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The Timing and Composition of Gestational Weight Gain and the Impact on Neonatal Anthropometry

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THE TIMING AND COMPOSITION OF GESTATIONAL WEIGHT GAIN AND THE IMPACT ON NEONATAL ANTHROPOMETRY

by

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In memory of Jonathan Woodrow

1957-2012

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Abstract

The Timing and Composition of Gestational Weight Gain and the Impact on Neonatal Anthropometry

Kathy Redfern

Background: Numerous maternal factors, such as body mass index (BMI), gestational weight gain (GWG), diet and physical activity (PA) have been shown to impact infant birth weight. In the UK, antenatal care tends to be based on pre-pregnancy BMI and women are not weighed routinely during pregnancy nor are there guidelines for GWG. However, it is widely acknowledged that maternal obesity and GWG in excess of the American Institute of Medicine guidelines are associated with increased risk of foetal macrosomia and recent studies have suggested a role of the timing and composition of GWG beyond that of BMI. The purpose of this study is to examine the effects of timing and composition of GWG on neonatal anthropometric outcomes in a prospective cohort study amongst women with a BMI≥30 kg/m^2 in Plymouth, UK.

Methods: Women (n=75) were recruited at 12 weeks gestation. Maternal height, weight and body composition assessed using skinfolds at biceps, triceps and subscapular were collected at baseline and repeated at 28 and 36 weeks gestation. Four-day food diaries and four days of accelerometry were collected in the days following each of the three study visits. Following delivery, infant weight and gestational age were obtained, and neonatal anthropometric measurements were recorded within 72 hours of delivery.

Results: Maternal energy intake was positively associated with GWG and rate of fat mass (FM) accrual, in the second ($r = 0.435$ and $r = 0.395$, respectively, $p<0.05$) and third trimesters ($r = 0.333$ and $r = 0.317$, respectively, $p<0.05$), with no associations observed between maternal energy intake and rate of fat free mass (FFM) accrual in either trimester. Maternal rate of FFM accrual (in both trimester 2 and over total pregnancy), not FM nor rate of GWG, was positively associated with infant birth weight z scores ($r = 0.360$ and $r = 468$, respectively, $p < 0.05$) and upper arm area muscle estimate (UME) ($r = 0.291$ and $r = 0.357$, respectively, $p < 0.05$). Second trimester intake of sugar was positively associated with infant UME ($r = 0.419$, $p<0.05$), while third trimester intake of sugar was positively associated with both infant UME and infant birth weight z score ($r = 0.376$ and $r = 0.308$, respectively, $p<0.05$).

Conclusion: The present study suggests that maternal accrual of FFM and intake of sugar during pregnancy may be associated with increased infant birth weight and lean mass. Further research is required to determine whether interventions should focus on changes in maternal body composition alongside diet and lifestyle during pregnancy, or if they should continue to focus on limiting total GWG.

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List of abbreviations

AC	Arm circumference
ADP	Air displacement plethysmography
AGA	Appropriate for gestational age
ANOVA	Analysis of variance
BIA	Bioelectrical impedance analysis
BMC	Bone mineral content
BMI	Body mass index
BMR	Basal metabolic rate
CHO	Carbohydrate
cm	Centimetre
CPM	Counts per minute
DLW	Doubly labelled water
DPA	Dietary pattern analysis
DRV	Dietary reference value
DXA	Dual x-ray absorptiometry
EI	Energy intake
FFM	Fat free mass
FFQ	Food frequency questionnaire
FM	Fat mass
g	Gram
GDM	Gestational diabetes mellitus

GI	Glycaemic index
GL	Glycaemic load
GWG	Gestational weight gain
GWL	Gestational weight loss
hsCRP	High sensitivity C-reactive protein
IOM	Institute of Medicine
Kcal	Kilocalorie
Kg	Kilogram
LBW	Low birth weight
LGA	Large for gestational age
LPA	Light physical activity
m	Metre
MET	Metabolic equivalent
MRI	Magnetic resonance imaging
MUAC	Mid-upper arm circumference
MVPA	Moderate or vigorous physical activity
NDNS	National Diet and Nutrition Survey
NHANES	National Health and Nutrition Examination Survey
NHS	National Health Service
OGTT	Oral glucose tolerance test

p	Probability
PCA	Principal components analysis
PPWR	Postpartum weight retention
r	Correlation
R&D	Research and Development
SD	Standard deviation
SDS	Standard deviation score
SFT	Skinfold thickness
SGA	Small for gestational age
TBF	Total body fat
TBW	Total body water
TOBEC	Total body electrical conductivity
UFE	Upper arm area fat estimate
UK	United Kingdom
UME	Upper arm area muscle estimate
US	United States of America
UWW	Underwater weighing
VPA	Vigorous physical activity
WT	Wear time

Conferences

Annual Student Conference – Nutrition Society. 7th-8th September 2017. University of Reading, UK (organising committee, oral presentation)

European Congress on Obesity – European Association for the Study of Obesity. 17th-21st May 2017. Porto, Portugal (poster presentation). Abstract published: Obesity Facts. 10 (Suppl.1): 147-148.

Annual Research Student Conference – Plymouth University Schools of Medicine and Dentistry PUPSMD. 30th March 2017 (poster and oral presentations).

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Annual Postgraduate Population Studies Conference (Popfest) - 6th-7th July 2015. Plymouth, UK (oral presentation).

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Workshops and seminars

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Publications

Redfern KM, Cammack VM, Sweet N, Preston, SoBHCS Student Team, Jarvis M & Rees G (2017) Nutrient-extraction blender preparation reduces postprandial glucose responses from fruit juice consumption. *Nutrition and Diabetes* 7, e288.

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Chapter 1 **General Introduction**

Obesity has become a worldwide epidemic, and in the United Kingdom (UK), it is estimated that half of women of childbearing age are classified as overweight or obese (Public Health England, 2013) and the prevalence of maternal obesity is increasing (Heslehurst *et al.*, 2009). It is well documented that maternal obesity has significant health implications for both mother and baby. Obesity increases the risk of miscarriage, gestational diabetes mellitus (GDM), gestational hypertension, thromboembolism and pre-eclampsia (Scott-Pillai *et al.*, 2013), and mothers with obesity are more likely to have prolonged pregnancies that require inducing or a caesarean section (Arrowsmith, Wray and Quenby, 2011). Women with obesity are less likely to breastfeed successfully (Mehta *et al.*, 2011) and tend to have longer stays in hospital after birth, which increases their risk of postnatal infections (Mamun *et al.*, 2011). Long term, women with obesity or excess weight gain during pregnancy, are more likely to remain obese postnatally (Rooney and Schauberger, 2002) and are also likely to increase their body mass index (BMI) with each subsequent pregnancy. Maternal obesity also carries a number of risks for the neonate including higher risk of stillbirth, congenital abnormalities, admission to the neonatal unit, and neonatal death (Dodd *et al.*, 2011). Offspring of mothers with obesity are also more likely to be born large for gestational age (LGA) or macrosomic (Bhattacharya *et al.*, 2007; Dodd *et al.*, 2011; Scott-Pillai *et al.*, 2013) which predisposes infants to adiposity and obesity during childhood (Whitaker, 2004; Margerison Zilko, Rehkopf and Abrams, 2010) as

well as increasing the risk of the development of metabolic syndrome (Boney *et al.*, 2005).

Excessive gestational weight gain (GWG) carries similar risks to maternal obesity for both maternal and neonatal outcomes (Nohr *et al.*, 2008; Mamun *et al.*, 2011). The Institute of Medicine (IOM) has therefore published recommendations for weight gain during pregnancy according to maternal pre-pregnancy BMI category (Rasmussen and Yaktine, 2009).

Both maternal obesity and excessive GWG are associated with increased risk of GDM (Scott-Pillai *et al.*, 2013; Li, Liu and Zhang, 2015), which has been shown to further increase the risk of excessive GWG and other adverse maternal outcomes such as maternal hypertensive disorders, caesarean section and induction of labour; as well as adverse infant outcomes such as macrosomia, low birth weight (LBW) and neonatal hypoglycaemia (O'Sullivan *et al.*, 2011).

Pregnancy is associated with increased nutritional needs, with nutritional status during pregnancy influencing important maternal and neonatal health outcomes such as GDM, maternal anaemia, hypertension, foetal growth and development, neural tube defects, infant cognitive and neurodevelopment, birth weight and potential long-term risk of childhood disease (Moran *et al.*, 2013). Although reports of food intakes during pregnancy across the general population have been variable (Rifas-Shiman *et al.*, 2006; Talai Rad *et al.*, 2011), there is evidence to suggest a decrease in diet quality during pregnancy amongst women with overweight or obesity (Laraia, Bodnar and Siega-Riz, 2007) that is maintained post-partum (Moran *et al.*, 2013). Recent studies examining dietary patterns in pregnancy have suggested an association between certain patterns

of food consumption and risk of excessive GWG, GDM and low or high birth weight (Hillesund *et al.*, 2014; Flynn *et al.*, 2016).

Recent retrospective cohort studies have shown that increased maternal and infant morbidity and hospital admissions as a consequence of raised BMI are leading to increased costs to the National Health Service (NHS) in the UK (Denison *et al.*, 2014; Morgan *et al.*, 2014). Costs in the first year of life, associated with increased healthcare service utilisation, were 72% higher amongst children born to mothers with obesity compared to those born to healthy weight mothers (Morgan *et al.*, 2015). Upon integration of these findings, Morgan and colleagues suggest that obesity during pregnancy costs an average of £2310 extra from conception to infant's first birthday and therefore suggest that interventions amongst women with obesity costing less than this figure, would be cost effective.

As demonstrated, women entering pregnancy with a raised BMI are at increased risk of numerous adverse consequences for themselves and their baby during pregnancy, delivery and postpartum (Scott-Pillai *et al.*, 2013). Women with obesity in Plymouth, UK are the focus of this work, and the primary aim of the thesis is to investigate the influence of maternal lifestyle factors: diet, physical activity and GWG, on infant birth weight and body composition amongst these women.

1.1 Summary of the thesis chapters

1.1.1 **Chapter 2: Review of the literature**

This chapter is divided into two sub-chapters. The first is a general review of the literature, exploring the impact of maternal obesity, GWG and lifestyle on maternal

and infant outcomes, with a particular focus on the primary outcome of the present study: infant birth size. The second is a semi-systematic review which was conducted in order to explore the current literature surrounding maternal dietary patterns and their impact on GWG, GDM and infant birth size. This semi-systematic review was also used to inform the methodology chosen to examine dietary patterns amongst the cohort of women in the present study.

1.1.2 **Chapter 3: Methodology**

In this chapter, the methods employed for the recruitment and follow-up of participants, and in the analysis of data are described and justified.

1.1.3 **Chapter 4: Description of the cohort**

The cohort of women in the present study are described and discussed in this chapter. This includes demographic information, baseline characteristics of the cohort and delivery information, which were compared to national data and data from similar studies amongst women with obesity. Trends in maternal anthropometrics, diet and physical activity across pregnancy are also examined and compared with observations from other studies.

1.1.4 **Chapter 5: Analysis of data**

Data relating specifically to the research questions the study sought to answer are presented in this chapter and discussed with reference to the body of literature. The research questions that this thesis seeks to answer are as follows:

1. How does diet affect maternal and infant outcomes?
2. How does physical activity affect maternal and infant outcomes?

3. Does the timing and composition of GWG affect infant birth weight and adiposity?

1.1.5 **Chapter 6: General Discussion**

This chapter includes a summary of the main findings from the present study, their potential implications and the limitations of the study. Finally, suggestions for future research to build on the findings from this work are given.

Chapter 2 **Review of the Literature**

2.1 General literature review

2.1.1 **Maternal obesity**

Obesity is generally defined as an excess accumulation of body fat that may impair health. As a proxy for excess body fat, which has been shown to correlate with excess body weight (Smalley *et al.*, 1990; Strain and Zumoff, 1992), BMI is used to classify individuals by their degree of underweight, or excess weight, relative to their height. BMI is calculated as weight in kilograms (kg), divided by height in metres (m) squared (kg/m^2) and is easy to obtain at population level. BMI cut-offs have been developed by the World Health Organisation in order to identify individuals at high risk of morbidity and mortality associated with excess body fat (World Health Orgnanisation, 1995). The international BMI categories are underweight (BMI <18.5 kg/m^2), normal range (18.5 kg/m^2 ≥ BMI < 24.9 kg/m^2), overweight (25 kg/m^2 ≥ BMI < 30 kg/m^2) and obese (BMI ≥30 kg/m^2). Obesity has been further classified to Class I (30.0 ≥ BMI <35.0 kg/m^2), Class II (35.0 ≥ BMI <40.0 kg/m^2) and Class III (BMI ≥ 40.0 kg/m^2).

BMI is not without its limitations, and is largely based on the assumption that BMI represents adiposity independently of age, sex and ethnicity, which have been shown to influence the relationship between BMI and adiposity (Gallagher *et al.*, 1996; Deurenberg, Yap and Van Staveren, 1998). In the UK, early pregnancy BMI is typically calculated at booking, and often dictates the care pathway that women receive. Many studies suggest that women gain minimal weight in the first trimester, and that early pregnancy BMI calculated at booking is an appropriate indicator of pre-pregnancy BMI

and thus excess adiposity (Rasmussen and Yaktine, 2009). However, Gilmore and Redman (2014) reported that using weight collected in the first trimester to calculate pre-pregnancy BMI resulted in misclassification of 1 in 10 women when compared to their true pre-pregnancy weight using data from Butte et al (2004). BMI calculated from an early pregnancy weight should therefore be interpreted with caution, as BMI does not account for any pregnancy-related changes such as plasma volume expansion, nor the growth of the uterus, breast tissue or foetus. However, despite its limitations, and in the absence of other anthropometric measurements, BMI calculated from a pre-pregnancy weight or before pregnancy-related GWG has occurred, is a useful clinical tool for identifying women at risk of overweight or obesity. A retrospective epidemiological study conducted across 34 maternity units in the UK suggested that the incidence of obesity (BMI ≥ 30.0 kg/m^2) at the start of pregnancy significantly increased between 1989 and 2007, from 7.6% to 15.6% (Heslehurst *et al.*, 2009). Recent data from the Health Survey for England (HSE) 2016 suggests that the prevalence of obesity amongst women aged 16-24, 25-34 and 35-44 years was 13%, 20% and 24%, respectively (Health and Social Care Information Centre, 2017). According to data collected by the Euro-Peristat Network, the proportion of women with a pre-pregnancy BMI ≥ 30 kg/m^2 ranges from 7.1% (Poland) to 20.7% (Scotland) across ten European countries, plus three regions of Belgium (Euro-Peristat, 2013). The prevalence of obesity amongst women of childbearing age appears to be considerably higher in the United States (US), with 37% of women aged 20-39 years with obesity (Hales *et al.*, 2017). In Plymouth, the recruitment location of the current work, 24.2% of all women entering pregnancy in 2017 had a booking BMI ≥ 30 kg/m^2 (clinical audit

data, unpublished), which appears to be considerably higher than rates observed across Europe in 2013 (Euro-Peristat, 2013), as well as the rates reported in the HSE for women aged 16-24 and 25-34 years (Health and Social Care Information Centre, 2017).

2.1.2 **Gestational weight gain**

Weight gain during pregnancy varies considerably between women, and has been shown to affect the immediate and future health of both mothers and infants (Kominiarek and Peaceman, 2017). In the United States, the IOM has published recommendations for GWG, which were updated in 2009 to include BMI-specific guidelines (Rasmussen and Yaktine, 2009; Table 2.1). The National Institute for Health and Care Excellence (NICE) does not currently make recommendations for GWG amongst the UK population, due to a lack of evidence-based guidelines (National Institute for Health and Care Excellence, 2010). Although the IOM recommendations were designed for the US population, the recommendations are largely based on evidence derived from the US and Europe, and thus, the IOM recommendations or similar, have been adopted in many other countries worldwide, although inconsistencies are apparent for many other countries (Scott *et al.*, 2014).

Table 2.1 Institute of Medicine gestational weight gain recommendations (Rasmussen and Yaktine, 2009)

	Total weight gain Range in kg	**Rates of weight gain 2nd and 3rd trimester Mean (range) in kg/week**
Underweight (BMI <18.5 kg/m^2)	12.5-18.0	0.51 (0.44 – 0.58)
Normal weight (18.5 kg/m^2 ≥ BMI < 24.9 kg/m^2)	11.5- 16.0	0.42 (0.35 – 0.50)
Overweight (25 kg/m^2 ≥ BMI < 30 kg/m^2)	7.0 – 11.5	0.28 (0.23 – 0.33)
Obese (BMI ≥ 30 kg/m^2)	5.0 – 9.0	0.22 (0.17 – 0.27)

Ideally, total GWG would be measured as the difference between maternal weight at conception and final weight just prior to delivery (Kominiarek and Peaceman, 2017). However, in practice, this is not always realistic, as most observational studies are not able to recruit participants until into the first trimester, by which point, substantial GWG may have already occurred. Total GWG reported in this way is also limited by the fact that total GWG is inherently positively correlated with gestational age at delivery (Hutcheon *et al.*, 2012). As well as total GWG, the IOM recommend weekly rates of GWG for the second and third trimesters. Reporting GWG as rate of GWG facilitates the comparison of GWG amongst pregnancies of varying durations and between research studies of various designs, and there appears to be a move in the literature towards reporting GWG in this way.

2.1.3 **Macrosomia and large for gestational age**

Macrosomia is generally defined as birth weight ≥4.0kg, or in some cases ≥4.5kg, irrespective of gestational age (Gaudet, Ferraro and Wen, 2014). It increases the risk of infant birth complications such as birth asphyxia and shoulder dystocia, thus increasing

the need for delivery via caesarean section, which carries its own risks to both mother and infant (Bérard *et al.*, 1998). Some studies report birth weight adjusted for sex and gestational age as birth weight percentile or standard deviation (SD or z-) score, with infants classified as LGA if their adjusted birth weight is ≥90th percentile as determined by population-specific datasets (Aye *et al.*, 2010). It is therefore important to establish the interactive effects of factors such as maternal obesity, GWG and dietary intake on the prevalence of macrosomia in order to develop effective strategies to reduce risk.

Maternal pre-pregnancy BMI has long been associated with increased risk of delivering a macrosomic infant or LGA in numerous studies. Mothers classified as overweight (BMI ≥25 and <30 kg/m^2), obese Class I (BMI ≥30 and <35 kg/m^2), Class II (BMI ≥35 and <40 kg/m^2) and Class III (BMI ≥40 kg/m^2) had increased odds ratios of 1.5 (99% CI 1.3, 1.6), 1.9 (CI 99% 1.6, 2.2), 2.1 (CI 99% 1.7, 2.6) and 3.2 (CI 99% 2.4, 4.1) of macrosomic infant, respectively, when compared with mothers classified as normal weight (BMI ≥18.5 and <25 kg/m^2) and adjusted for gender and gestational age in Northern Ireland (Scott-Pillai *et al.*, 2013). Similar patterns of increased risk with increasing BMI were observed in other studies in Scotland (Bhattacharya *et al.*, 2007) and Australia (Dodd *et al.*, 2011) and provide strong evidence that maternal obesity confers an increased risk of infant macrosomia when BMI alone is examined.

In 2008, the Agency for Healthcare Research and Quality performed a systematic review of outcomes relating to GWG in which they observed a consistent positive association between higher GWG and infant birth weight (Viswanathan *et al.*, 2008). Although definitions varied between studies, they also generally observed increased risk of macrosomia with increasing GWG, and for ten studies that reported GWG and

LGA, reported that risk of LGA increased by a factor of 1.1 for each 1kg increment in GWG. This particular review was used to inform the 2009 IOM GWG guidelines (Rasmussen and Yaktine, 2009). There is now extensive evidence supporting the independent relationship between both obesity and GWG and birth size, so studies have tended to examine joint associations between BMI and GWG and for those published post-2009, adherence to IOM guidelines.

2.1.4 **Impact of maternal obesity and gestational weight gain on infant birth weight**

A retrospective cohort study evaluated the effects of GWG on maternal and neonatal outcomes in different BMI classes (Crane *et al.*, 2009). In keeping with findings from previous studies, they observed that mothers classified as overweight or obese were significantly more likely to give birth to a macrosomic infant than normal weight mothers. They were also significantly more likely to gain excess weight than mothers with a normal BMI, however, when the impact of GWG on risk of macrosomic infant was examined by BMI class, an increased risk was observed with excess GWG for all BMI classes, compared with GWG within the guidelines, with adjusted odds ratios of 1.21, 1.30 and 1.20 for healthy weight, overweight and obese mothers, respectively. These findings suggest that although women with overweight or obesity are at increased risk of macrosomic infant and of gaining excess weight, when excessive GWG does occur, risk of macrosomic infant increases regardless of pre-pregnancy BMI category. The main limitation of this study was that it was of a retrospective nature, and so pre-pregnancy BMI or GWG data were missing for 47.8% of women who met all other inclusion criteria, suggesting potential for inclusion bias. A similar study, published in 2008, reported that BMI category was a stronger predictor of LGA

neonate than GWG, but that very high GWG (defined as >20kg) increased the absolute risk of LGA neonate across all BMI categories (Nohr *et al.*, 2008). However, major limitations of the study were that pre-pregnancy weight and height were self-reported, and GWG was self-reported six months postnatally via telephone interview, which increases potential for self-report bias. Both of these studies were conducted or published prior to the release of new BMI-specific IOM recommendations for GWG (Rasmussen and Yaktine, 2009), so categories of GWG were therefore defined according to prior guidelines (Institute of Medicine, 1990b) which does limit their transferability somewhat.

Compared with adequate GWG, excessive GWG according to IOM 2009 guidelines more than doubled the risk of LGA (Margerison Zilko, Rehkopf and Abrams, 2010). Risk of LGA was higher for overweight and obese women, regardless of GWG, and when GWG was taken into account in multivariate analysis, increased GWG increased the probability of LGA. Similarly, maternal BMI alone, and the interaction between maternal BMI and GWG were both significantly associated with infant growth trajectory, as defined by weight-for-length percentile (World Health Orgnanisation, 2006), from birth through to 12 months, while GWG alone did not reach significance in a recent study amongst US women (Heerman *et al.*, 2014). In particular, maternal morbid obesity (BMI ≥40 kg/m^2) was significantly associated with infant growth trajectory throughout the first 3 months of life, and further amplified by excess GWG. At 12 months of age these effects were sustained, while infants born to mothers with a healthy BMI, but with excess GWG, had normalised their growth by this point.

A prospective study indicated that pre-pregnancy BMI and excessive GWG, according to IOM 2009 guidelines in all BMI classes, should be considered independent predictors of macrosomia, but that no interaction between the two variables was observed (Alberico *et al.*, 2014), with similar findings observed in another study (Dietz, Callaghan and Sharma, 2009). However, neither study examined women by obesity class, so as the authors acknowledge, this could explain the absence of interaction. A recent systematic review analysed studies that had stratified women by severity of obesity and GWG according to the current IOM guidelines (Faucher and Barger, 2015). The authors concluded that optimum GWG, in order to decrease the risk of LGA, without increasing the risk of small for gestational age (SGA), should remain at 5-9kg GWG for women in Class I, but decrease to 1-5kg GWG for women in Class II and to no GWG for women in Class III. It is clear from these studies that further work is required in women with obesity to determine optimal GWG, as well as reduce risk of excessive GWG and foetal macrosomia/LGA.

2.1.5 **Timing of gestational weight gain**

Although the influence of total GWG during pregnancy has been well documented, the timing of overnutrition and subsequent weight gain has not been examined as thoroughly. Davenport et al. (2013) evaluated whether the timing of excessive GWG in pregnant women following current healthy living guidelines affected neonatal adiposity at birth in their prospective cohort study. The cohort were retrospectively grouped according to IOM GWG guidelines in the first and second halves of pregnancy. Infants born to women who exhibited excessive GWG during the first half of pregnancy ("early excessive" and "overall excessive") exhibited greater birth weight, crown-heel

length and neonatal FM compared with infants born to women who exhibited appropriate GWG during the first half of pregnancy ("overall appropriate" and "late excessive"). These differences remained significant after controlling for confounders and posthoc regression analyses demonstrated that the equation including timing of GWG better predicted neonatal body fat (R^2 = 0.328, <0.010) than the equation including total GWG (R^2= 0.077, p=0.034). Starling et al. (2015) observed that maternal BMI and GWG were positively and independently associated with infant FM, FFM and percentage body fat, as assessed by air displacement plethysmography (ADP). Trimester-specific rates of GWG were also examined with early-, mid- and late-pregnancy rates of GWG independently associated with infant FM and percentage body fat, and mid- and late-pregnancy rates of GWG independently associated with infant FFM.

Farah et al (2011) observed that birth weight significantly correlated with GWG before the third trimester (r=0.163, P=0.027) but not with total GWG nor GWG in the third trimester while another recent study found that high GWG prior to 20 weeks was positively associated with risk of LGA, regardless of later GWG (Catov *et al.*, 2015). Another recently published study, using data obtained between 1991 and 1993, observed that high rate of GWG, as defined by tertiles, in the second trimester was associated with higher infant birth weight and length, with no associations between GWG in the first or third trimesters and infant birth size (Widen *et al.*, 2015). Hivert and colleagues (2016) observed a positive association between rate of GWG in all three trimesters and birth weight z-score, although the largest effect size was observed for second trimester GWG.

These data suggest that neonatal birth size is more strongly influenced by timing of GWG than total GWG, with mixed findings reported amongst the studies above. GWG in the second trimester appears to most consistently influence infant birth weight, however, data on GWG in the first trimester is limited, as observational studies tend to recruit during, or towards the end of the first trimester, which is a difficult limitation to overcome, unless women can be recruited prior to conception. The time periods examined also varies considerably between studies, which makes comparison difficult. Studies examining rates of GWG at frequent assessments are therefore required in order to increase our understanding of the importance of GWG during different stages of pregnancy and to enable the development of transferable recommendations.

2.1.6 **Composition of gestational weight gain**

Although BMI is widely used to provide estimates of body composition, it is not without its limitations and GWG is typically reported as a single measure of mass gained during pregnancy, with the individual effects of FM and FFM gains left unexplored. Prentice and Jebb (2001) propose that obesity should be defined as the excess accumulation of body fat, whereas BMI and GWG identify the presence of excess or additional body weight, which may not necessarily confer excess body fat and obesity, nor increase the risk of comorbid conditions. In pregnancy, protein, fat, water and minerals are deposited in foetal and maternal tissues and contribute to GWG as proposed by Pitkin (1976) and shown in Figure 2.1. The extent to which these components influence maternal and foetal outcomes is not fully understood and so, the impact of maternal body composition - as measured by estimation of body fat - on

pregnancy outcomes in addition to GWG and maternal obesity as defined by BMI, should therefore be explored.

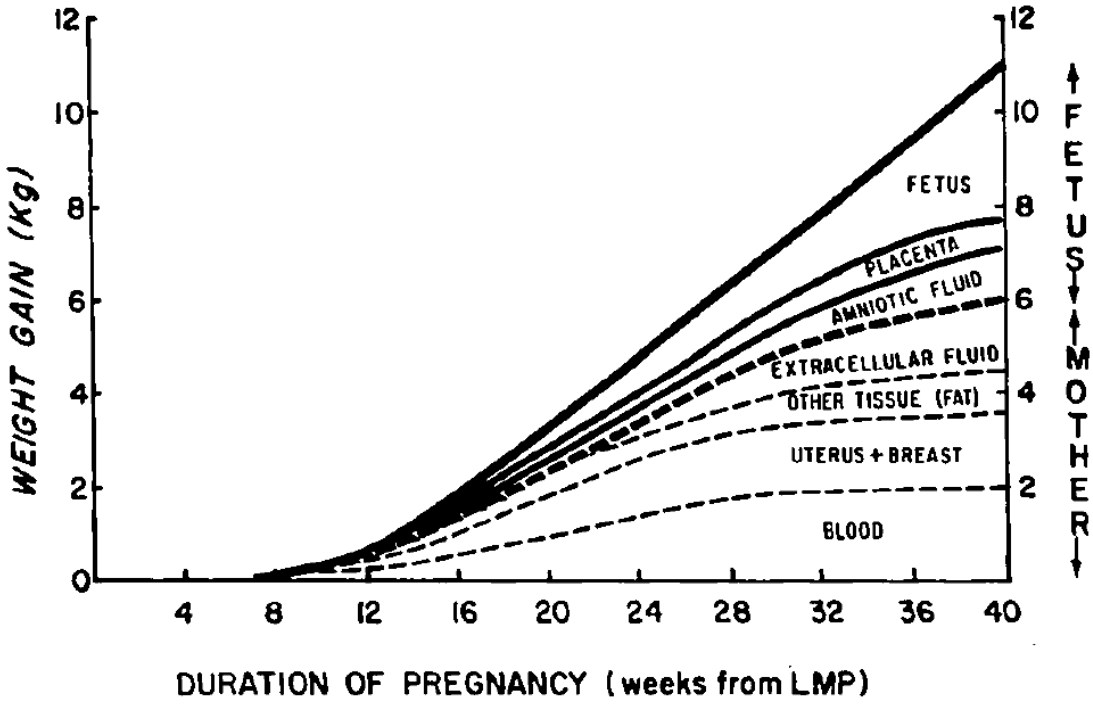


Figure 2.1 Pattern and components of gestational weight gain during pregnancy (Pitkin, 1974)

2.1.6.1 Methods of assessing maternal body composition

There are numerous methods available for the estimation of body composition amongst the general population, many of which may be adapted for use with pregnant women. According to a review from Widen and Gallagher (Widen and Gallagher, 2014), anthropometry, is the most commonly used method for assessing body composition during pregnancy due to it being portable, inexpensive and simple to implement. Anthropometric measurements in pregnancy typically involve SFT measurements, combined with arm circumference (AC), and can be used to give regional or total body estimates of FM and FFM with the use of various equations.

Many equations have been validated for use at specific gestational ages (Paxton *et al.*, 1998; Huston Presley *et al.*, 2000), and thus cannot be used to assess changes in body composition over pregnancy. Other equations have been developed for use throughout pregnancy (Kannieappan *et al.*, 2013) or SFT measurements can be used themselves to assess changes over time, rather than using equations to estimate FM and FFM. In all populations, SFT is influenced by the compressibility of subcutaneous adipose tissues which can vary by site, gender, age, weight changes, and pregnancy, with some evidence to suggest an increase in compressibility across pregnancy due to changes in hydration of subcutaneous adipose tissue (Robertson, 1969). However, the degree to which compressibility varies across different pregnant populations and SFT sites, is not fully understood. SFT measurements can also be subject to measurement error, due to a lack of reliability or accuracy (Ulijaszek and Kerr, 1999). Use of an experienced anthropometrist, repeated measurements and calibrated skinfold callipers can reduce the prevalence of measurement error.

Bioelectrical impedance analysis (BIA) is another example of a two-compartment model that can be used to estimate FM and FFM from TBW estimates based on the resistance of tissues to electrical flow. Similarly to anthropometry, BIA is commonly used in observation studies as they are portable, inexpensive and simple to use.

The use of a four-compartment model is considered the gold-standard for assessing body composition during pregnancy which is based on FM, total body water (TBW), bone mineral content (BMC) and protein (Widen and Gallagher, 2014). Estimates of FM or FFM are frequently obtained from estimates of body density, which may be estimated using underwater weighing (UWW) or ADP techniques, although as they

require specialist equipment and settings, are not suitable for field research. TBW is typically measured using the dilution principle using water labelled with an isotope. This technique is known as doubly labelled water (DLW). Although unsuitable for use during pregnancy, due to radiation exposure, DXA may be used before or after pregnancy in order to estimate BMC, as the fourth compartment. Although considered the gold standard, the four-compartment model cannot distinguish between maternal and foetal tissues, and is not commonly used in cohort studies of pregnancy due to costs associated with performing these techniques.

A prospective observational study conducted by Farah et al (2011) observed that maternal weight, FFM and FM, as assessed via BIA, increased between 28 and 37 weeks gestation. However, only maternal FFM, and not maternal FM was significantly correlated with infant birth weight at either time-point. A similar study conducted by the same research group, also used BIA to assess maternal body composition parameters, this time, in the first trimester only (Kent *et al.*, 2013). In multivariable regression analysis, FFM, but not FM was a significant predictor of birth weight, and after adjustment for confounding variables, mothers in the highest FFM quartile were at significantly higher risk of macrosomia compared with mothers in the lowest quartile. A similar and more recent prospective study conducted amongst Chinese women observed a similar relationship between maternal FFM, but not FM, and infant birth weight (Wang *et al.*, 2017).

Butte et al. (2003) partitioned GWG into FM, FFM, total body water and protein gains as assessed by a multicomponent model at weeks 9, 22 and 36 of gestation. FFM gains at all three time points and TBW gains in the second and third trimester were found to

make independent contributions to birth weight, while FM was not related to birth weight at any time point.

These studies suggest FFM, and not FM mediates an increase in infant birth weight. Maternal plasma volume expansion has been positively associated with infant birth weight in both human and animal studies (Rosso, 1990), which may explain the associations between maternal FFM and/or TBW and infant birth weight described in the studies above. Most of these studies employed BIA to assess maternal body composition, which is unable to distinguish between the maternal and foetal unit. The weight of the foetus may therefore be contributing to maternal FFM and acting as a confounding factor in the association between GWG and infant birth weight. A recent observational study, conducted in Ireland, suggests that when infant birth weight is subtracted from total GWG, the positive correlation between GWG and birth weight no longer exists (O'Higgins et al, 2018), so it is possible that the weight of the foetus is also acting as a confounding factor when GWG is examined as FM and FFM.

Forsum et al. (2006) addressed their hypothesis that maternal body fat content stimulates growth of the foetus and its adipose tissue in a small, observational study. They assessed infant subcutaneous adipose tissue volume in vivo using magnetic resonance imaging (MRI), while maternal body composition was assessed using a two-compartment model based on TBW. It was observed that maternal TBF before pregnancy and at 32 weeks gestation were significantly and positively correlated with infant birth weight, while in infants, birth weight positively correlated with subcutaneous adipose tissue. In multiple regression analysis, TBF before pregnancy and infant subcutaneous adipose tissue together, and TBF at week 32 of gestation and

infant subcutaneous adipose tissue together were significant predictors of infant birth weight (R^2 = 0.61, P=0.00003; R^2 = 0.63, P=0.00002, respectively).

Of these studies only Forsum et al. (2006) examined neonatal body composition, while only Kent et al. (2013) specified an association between body composition and macrosomia, so it is not necessarily clear whether increased gains in FFM or FM are associated with LGA or macrosomia. Further studies examining the effects of maternal body composition changes throughout pregnancy on neonatal body composition and LGA/macrosomia are therefore required.

2.1.7 **Neonatal body composition**

2.1.7.1 Methods of assessing neonatal body composition

Maternal obesity has not only been associated with infant birth weight and macrosomia, but also with neonatal body composition, which unlike birth weight, can provide an estimation of the relative contributions of fat mass (FM) and fat free mass (FFM), which are important indicators of nutritional status.

ADP using PeaPod, which is suitable for infants up to 6 months of age and uses whole body densitometry, has been shown to reliably estimate infant FM and FFM and has been validated against deuterium dilution (Ma *et al.*, 2004) and the four compartment (4C) model (Ellis *et al.*, 2007). The advantage of ADP is that it is quick and portable within a hospital setting, meaning reduced burden is placed on researchers, parents and infants compared with a 4C model. However, the equipment is expensive and not so portable that it can be used in the field (Demerath and Fields, 2014). Dual x-ray absorptiometry (DXA) is a frequently reported method for assessing body composition amongst infants and has the advantage that FM, lean tissue and bone can all be

measured. However, like ADP, DXA measurements tend to be limited to hospital settings, and with DXA there is the disadvantage of exposure (although negligible) to radiation, and the infant is also required to lie still, which is often difficult to achieve. Variations between DXA manufacturers, models and software also makes comparison with reference data difficult, and although DXA and ADP estimates of body composition have been shown to be highly correlated, significant differences were present (Fields *et al.*, 2012).

Skinfold thickness (SFT) is a simple and non-invasive way of measuring FM in neonates, although it works on the assumption that subcutaneous FM is proportional to total body fat (TBF), which may not be the case (Rigo, 2006). Cauble et al. (2017) observed poor agreement between FM estimated from four newborn SFT equations and FM measured using ADP PeaPod and concluded that new prediction equations for estimating FM in newborns are desperately needed. Like SFT, BIA or total body electrical conductivity (TOBEC) are portable and non-invasive methods of assessing body composition amongst infants, although TOBEC is less frequently reported, as the equipment is no longer being manufactured. Like SFT, prediction equations for use with BIA and TOBEC have their limitations, and tend to perform poorly across different ethnic groups and stages of development, generally limiting their use at individual level (Demerath and Fields, 2014).

In addition to examining the effect of maternal obesity and GWG on infant birth weight, Carlsen et al (2014) added neonatal body composition as an outcome measure as assessed using DXA. They observed that infants born to mothers with obesity were significantly heavier than infants born to normal weight mothers, and this was

exclusively due to increased FM, with no difference in FFM. GWG on the other hand, was found to increase FM, percentage FM and FFM, with infants born to women exceeding GWG guidelines exhibiting significantly higher percentage FM than those born to women gaining within and below the guidelines. These findings concur with those observed by Crozier et al. (2010) who also observed significantly greater FM amongst infants born to women who exceeded IOM GWG guidelines compared to those gaining adequate weight, with no differences observed for infant FFM. Waters et al. (2012) identified significantly greater FFM, FM and percentage body fat for infants born to women exceeding IOM guidelines compared to women gaining within or below recommendations, however, when examined by BMI category, the relationship between GWG and infant body composition only remained for women with a healthy BMI pre-pregnancy.

Sewell et al. (2006) compared body composition between neonates born to lean/normal weight women and neonates born to mothers with overweight or obesity. Body composition was assessed within 72 hours of delivery using skinfold measurements and by TOBEC. A significantly higher rate of macrosomia and increased triceps, subscapular and flank SFT was observed in infants born to mothers in the overweight/obese group compared to mothers in the lean/normal weight group. There were no significant differences in infant FFM as measured by TOBEC between groups (2951 vs 3023 g, P= 0.22), however, infant FM and infant percentage FM were significantly higher for the overweight/obese mothers than for the lean/healthy weight mothers (406 vs. 331 g; P=0.008; and 11.0% vs. 9.6%; P = 0.006). There was also a significant correlation between GWG and infant percentage body fat (r= 0.35; P=0.003)

in the overweight/obese group only, with no correlation between GWG and infant FFM in this group (r=0.08; P=0.51).

Hull et al. (2008) observed that compared with infants of normal weight mothers, infants born to mothers with obesity had significantly greater percentage fat and FM, and significantly lower FFM, as measured by PeaPod ADP. This study was followed up to explore the impact of appropriate vs. excessive GWG, according to IOM 2009 guidelines, on infant body composition – once again measured by PeaPod ADP (Hull *et al.*, 2011). Within the appropriate GWG group, infants born to mothers with obesity had significantly greater percentage fat and total FM than those born to both overweight and normal weight mothers. Within the excessive GWG group, infants born to normal weight mothers had significantly lower percentage fat and FM than infants born to mothers with overweight or obesity. Differences in percentage fat and FM between GWG categories by BMI category were significantly greater for overweight mothers only. This study suggests that mothers with obesity had infants with greater adiposity regardless of whether they adhered to or exceeded IOM GWG guidelines, although did not report any findings for women who may have gained below IOM guidelines due to the sample size.

McCloskey et al (2016) observed a positive association between maternal BMI and infant birth weight and adiposity, in line with previous studies (Sewell *et al.*, 2006; Hull *et al.*, 2008), as well as a positive association between maternal BMI and cord blood high sensitivity C-reactive protein (hsCRP), an inflammatory marker. The authors hypothesised that these associations between maternal BMI and infant adiposity and inflammation may be mediated by maternal inflammation, as they also observed a

positive association between maternal hsCRP and cord hsCRP, and inclusion of maternal hsCRP as a covariate in regression analysis attenuated the associations between maternal BMI and infant adiposity and inflammation. McIntyre et al. (2010) reported a positive association between maternal BMI and foetal hyperinsulinemia – as assessed by cord serum C-peptide levels ≥90th percentile. Risk of birth weight and body composition ≥90th centiles also increased with increasing BMI category.

2.1.8 **Gestational diabetes mellitus**

It has long been documented that infants born to mothers with GDM are more likely to be LGA, with frequency of LGA infants in women with GDM reported to be between 25% and 45% (Kitzmiller, 1986). A recent prospective study conducted in Italy aimed to evaluate the role of GDM, alongside pre-pregnancy BMI and GWG on macrosomia risk (Alberico *et al.*, 2014). The authors concluded that all three risk factors should be considered independent risk factors for macrosomia, and that amongst women who developed GDM, excessive GWG significantly increased the risk of macrosomia compared to women gaining within or below IOM guidelines, which also agrees with findings from another recent study amongst Chinese women (Miao *et al.*, 2017). Durnwald et al. (2004) conducted a study to compare infant body composition, as assessed by TOBEC, of LGA infants born to GDM mothers compared with LGA infants born to mothers with normal glucose tolerance levels. Infants of mothers with GDM had increased FM (622 vs. 563g; P=0.02) and percentage body fat (16.2% vs. 13.5%; p<0.01), but decreased lean body mass (3400 vs. 3557g; p<0.01) compared with infants of mothers with normal glucose tolerance levels, despite no significant differences in birth weight between groups. Stepwise regression analysis of the entire

population showed that a diagnosis of GDM alone significantly correlated with neonatal percentage body fat (R^2 = 0.12; P<0.01).

2.1.9 **Long-term consequences of infant macrosomia**

There is evidence to suggest that infant macrosomia and adiposity at birth are associated with a number of long-term adverse consequences for offspring later in life including obesity, altered body composition and cardiometabolic disease (Drake and Reynolds, 2010).

2.1.9.1 Offspring obesity

A retrospective cohort study conducted in the United States observed that risk of LGA was significantly higher amongst infants born to mothers with obesity compared with healthy weight mothers (12.4% vs 6.3%; P <.001); and that LGA offspring were more than twice as likely to be classified as obese (BMI ≥ 95th percentile) when compared with appropriate for gestational age (AGA) offspring (20.5% vs 9.1%; P<0.001; Whitaker, 2004). The overall relative risk of obesity amongst children born to mothers with obesity was 2.0 (95% CI: 1.7-2.3) when compared to a reference group of healthy weight mothers. Similarly, Bider-Canfield and colleagues (2017) identified that odds of childhood overweight at 2 years (BMI ≥ 85th percentile) were significantly greater amongst children born to mothers with obesity, excessive GWG and GDM. Gale et al. (2007) examined the relationship between maternal size during pregnancy and body composition of their offspring at 9-years. They observed that offspring FM index (FM as measured by DXA and adjusted for height) at 9 years was greater in children whose

mothers had higher pre-pregnancy BMI and larger mid-upper AC (MUAC) in late pregnancy, suggesting childhood adiposity is positively affected by maternal obesity. A recent meta-analysis examined the influence of excessive GWG according to IOM guidelines on offspring obesity at different stages in life (Mamun, Mannan, & Doi, 2014). Risk of offspring obesity in childhood, adolescence and adulthood was significantly higher amongst offspring born to women exceeding GWG guidelines compared to those born to women gaining weight within the guidelines. Hivert and colleagues (2016) examined data from the Project Viva cohort on the impact of the timing of GWG on mid-childhood body composition and observed that rate of GWG in the first and second trimesters was positively associated with BMI z-score, FM and FFM, while rate of third trimester GWG was not associated with childhood adiposity. These findings agree with those observed amongst offspring from the Danish National Birth Cohort where rate of GWG in the first and second trimester, but not the third, were positively associated with BMI z score at 7 years (Andersen *et al.*, 2011). Bayer and colleagues (2014) observed a positive effect of rate of GWG in all three trimesters on childhood BMI z score and waist circumference, with the strongest effect observed in the second trimester.

2.1.9.2 Offspring cardiometabolic disease risk

Offspring of women who gained in excess of IOM GWG recommendations had significantly higher BMI, waist circumference, FM, leptin, CRP and systolic blood pressure at age 9 than offspring of those who gained within IOM recommendations in a large UK prospective cohort study (Fraser *et al.*, 2010). Offspring of women who gained below IOM guidelines had lower levels of adiposity, but other cardiovascular

risk factors were similar to those of offspring born to women exceeding guidelines, and none of these associations appeared to be modified by maternal pre-pregnancy BMI or body weight.

Boney et al. (2005) examined the development of metabolic syndrome in LGA and AGA offspring of mothers with and without GDM. The prevalence of metabolic syndrome was significantly greater amongst offspring in the LGA/GDM group (50%) than for the LGA/control group (29%), AGA/GDM group (21%) and the AGA/control group (18%), with no other significant differences between groups. A Swedish study investigated the impact of birth weight on risk of metabolic diseases in adulthood (Johnsson *et al.*, 2015). For adult men, risk of type 2 diabetes was increased 1.9-fold for those with birth weights between 2 and 3 standard deviation scores (SDS) and 5.4-fold for those with birth weight greater than 3 SDS, compared with those with birth weight -2 to 2 SDS.

2.1.10 **Maternal Lifestyle**

2.1.10.1 Maternal Diet

Nutritional status prior to and during pregnancy influences growth and development of the foetus, GWG and general maternal health (Institute of Medicine, 1990a). There is significant interest in the role of maternal dietary intake on excessive GWG, adverse pregnancy outcomes and infant birth size outcomes, particularly amongst women with obesity, for whom risk of adverse outcomes is greatest.

2.1.10.2 Diet and gestational weight gain

A prospective cohort study in the US using data from Project Viva sought to identify modifiable diet and physical activity risk factors for excessive GWG – as defined by IOM guidelines (Stuebe, Oken and Gillman, 2009). In multivariable logistic regression they found that total intake of energy, dairy and fried foods were directly associated with excessive GWG, while first trimester vegetarian diet, mid-pregnancy walking and vigorous physical activity (VPA) decreased the risk of excessive GWG. How these reductions in GWG translated to neonatal outcomes was not examined. Bärebring and colleagues (2016) examined four day food records of Swedish women in their third trimester and observed intakes of caloric beverages, snacks, fish, bread and dairy to be positively associated with GWG, and with the exception of dairy, higher odds of excessive GWG.

An observational study conducted in Iceland aimed to identify dietary factors from FFQ data related to excessive GWG as classified by Icelandic recommendations of 12.1-18.0kg for women with a healthy BMI, and 7.1-12.0kg for women classified as overweight (Olafsdottir *et al.*, 2006). For women with a healthy BMI, dietary intake did

not differ between GWG groups, while overweight women who exceeded GWG guidelines had significantly higher energy intake (EI), higher percentage energy from fat, and lower percentage energy from carbohydrate, than overweight women with suboptimal GWG. Although infant birth weight was significantly higher for mothers gaining adequate and excessive GWG, compared with mothers with suboptimal GWG, the relationship between infant birth weight and dietary intake was once again, not examined. Lagiou et al. (2004) examined the impact of maternal energy-adjusted intake of macronutrients on GWG and birth-size parameters in a prospective cohort of 224 US women using a FFQ. Similarly to the studies reported above, GWG was significantly and positively associated with EI, as well as energy-adjusted intakes of lipids from animal origin and protein. There was also a significant inverse association between carbohydrate intake and GWG. Despite well-documented associations between GWG and birth size, no associations between energy or macronutrient intakes and birth size were identified. The relationship between protein-to-carbohydrate (P/C) ratio and added sugar in mid-pregnancy and GWG were examined in the Danish National Birth Cohort (DNBC) (Maslova *et al.*, 2015). Women in the highest P/C quintile exhibited significantly lower rate of GWG compare to women in the lowest quintile, as did women with greater than 20% of their energy coming from protein, compared to those with less than 12%. A high P/C ratio was inversely associated with intake of added sugars, and the authors hypothesised that the association between P/C ratio and GWG was driven by a decrease in added sugars. The authors also reported that when fat was substituted for carbohydrate to give a

protein-to-fat ratio, results were similar, although slightly weaker, but these results were not published in the manuscript.

Findings from the studies reported above are conflicting, and other than generally observing positive associations between EI and percentage energy from fat and GWG, these studies do not reach a consensus on the impact of carbohydrates and protein on GWG. This may be in part due to the majority of the studies relying on FFQs, which may be restricted by measurement error (Shim, Oh and Kim, 2014).

2.1.10.3 Diet and infant birth size

Animal studies have shown a consistently positive relationship between maternal dietary intake of fat, offspring adiposity and metabolic dysfunction (Ribaroff *et al.*, 2017). Human studies have generally been less conclusive in their observations, in large part due to methodological inconsistencies and limitations.

The Healthy Start Study, a prospective cohort study set in the US observed a positive and significant association between maternal intakes of carbohydrate, total, saturated and unsaturated fat and infant FM, with no association observed between intakes and birth weight or FFM (Crume *et al.*, 2016). There was also a positive association between protein intake and infant FM, although not quite significant, suggesting that most forms of increased EI contribute to increased infant fat deposition, regardless of macronutrient composition. An Australian study examined the relationship between maternal diet and intrauterine development of foetal body composition, observing a positive association between protein and starch intakes and P/C ratio and infant abdominal fat percentage, while maternal intake of saturated fat was positively associated with mid-thigh fat (Blumfield *et al.*, 2012). Another Australian study

reported a positive association between maternal percentage energy from protein in early, but not late, pregnancy and birth weight and ponderal index, independently of GWG and total EI. Percentage energy from carbohydrate was inversely associated with ponderal index in late, but not early pregnancy (Moore *et al.*, 2004).

The aim of a large, prospective cohort study conducted by Olsen et al. (2007) was to examine the influence of milk consumption on infant birth size, once again using data from the DNBC. Milk consumption was inversely associated with SGA, and directly associated with LGA and mean birth weight, with women consuming ≥ 6 glasses of milk/day exhibiting increased risk of LGA (OR 1.59, 95% CI 1.16, 2.16) when compared with women who reported no milk consumption. When fat and protein intakes from dairy products (excluding cheese and ice cream) were examined, there was a positive association between protein intake and birth weight, with no association observed for fat. The authors proposed that the positive association between milk consumption and birth weight is driven by the presence of insulin-like growth factor-1 (IGF-1) in both low-fat and whole-milk products.

The mechanism by which maternal obesity and/or excess weight gain may confer obesity in offspring is not entirely clear. One proposed mechanism is the 'developmental overnutrition hypothesis' which suggests that the foetus is exposed to high concentrations of maternal glucose and free fatty acids, as these nutrients cross the placenta easily, resulting in increased foetal secretion of insulin, thus leading to increased risk of adiposity (Drake and Reynolds, 2010). The lack of consensus regarding carbohydrate intake and GWG discussed above may be because some studies looked at total carbohydrate intake, rather than distinguishing between

sources of carbohydrate. It is well-documented that glucose in the major substrate for foetal growth, and thus may be associated with foetal overgrowth (Herrera, 2000). Another study from the DNBC examined the associations between maternal dietary glycaemic load (GL), GWG, birth weight and risk of LGA neonate (Knudsen *et al.*, 2013). Women in the highest GL quintile had significantly greater GWG, birth weight, and increased risk of LGA compared with women in the lowest quintile, although when examined by BMI category these associations tended to disappear.

Secondary analysis of data from the TOP (Treatment of Obese Pregnant women) study set in Denmark observed a significant positive relationship between maternal intake of digestible carbohydrate in late, but not early pregnancy and infant percentage body fat (Renault *et al.*, 2015). Women in the highest quartile of carbohydrate intake also had infants with significantly greater percentage body fat, compared with women in the lowest quartile, once again in late, but not early pregnancy. However, when stratified by 2-hour OGTT values, no significant association between carbohydrate intake and infant fat percentage remained for women with well-controlled glucose (OGTT ≤6.6 mmol/L), but the association was once again significant, and increased in strength with higher intolerance (OGTT values 6.7-7.7 and ≥7.8 mmol/L). These findings suggest that even in the absence of GDM, carbohydrate intake may influence FM of infants born to women with obesity and impaired glucose tolerance.

There is also evidence to suggest overnutrition during pregnancy results in metabolic imprinting affecting the hypothalamus, adipose tissues and pancreatic islet cells of the offspring, which may lead to an increased predisposition to obesity throughout offspring life course via a number of pathways which may include, but are not limited

to: appetite regulation, altered metabolic rate, altered adiposity and adipocyte metabolism (Taylor and Poston, 2007). As well as the impact of the intrauterine environment on offspring obesity, which may be mediated by such factors as maternal obesity, maternal body composition, GWG and maternal diet, the inheritance of genes which may confer susceptibility to obesity and the maternal role in raising a child in a potentially obesogenic environment must also be considered (Drake and Reynolds, 2010).

2.1.10.4 Diet and physical activity

There is an increasing interest in the promotion of physical activity during pregnancy, not only in relation to reducing excessive GWG, but also for its potential to improve pregnancy outcomes for both mother and neonate (McParlin *et al.*, 2010). It is well documented that pregnant women appear to compensate for the increased energy demands of pregnancy via a decrease in physical activities (Rousham, Clarke and Gross, 2006; Lof, 2011), with women with obesity shown to exhibit larger declines in physical activity over pregnancy than women with a healthy BMI (Sui, Moran and Dodd, 2013). Clapp & Little (1995) observed the effect of recreational exercise throughout pregnancy on GWG and subcutaneous fat deposition. GWG and subcutaneous fat deposition were reduced in those who continued to exercise in the third trimester, with no changes observed earlier in pregnancy, suggesting that physical activity influences late, but not early GWG and subcutaneous fat deposition. Similarly, Norwegian women who exercised regularly (≥1 times per week), had lower GWG than inactive women, although once again, this was significant in the third trimester only (Haakstad *et al.*, 2007). A later study, conducted by the same authors, suggests that

many women avoid exercise in the third trimester (Haakstad *et al.*, 2009), suggesting that perhaps maintenance of physical activity in the third trimester should be a focus of pregnancy lifestyle interventions. In keeping with these findings, Ruifrok et al. (Ruifrok *et al.*, 2014) observed a decrease in time spent in moderate or vigorous physical activity (MVPA) from early to late pregnancy, but no relationship between MVPA or sedentary behaviour at either time point and GWG or infant birth weight. No differences in physical activity assessed by accelerometer were observed between intervention or control arms in a pilot of the UPBEAT trial in the UK (Hayes *et al.*, 2014). However, when data from women in both arms of the study were combined, women who gave birth to macrosomic babies (birth weight ≥4.0kg) spent significantly less time at baseline in light physical activity (LPA) than those who had babies not classified as macrosomic, while time spent in sedentary activity was inversely associated with infant abdominal circumference, which was used as a proxy for abdominal adiposity. For activity at the end of the third trimester, time in sedentary activity was positively associated and time in both LPA and MVPA were inversely associated with infant abdominal circumference. Data from the Healthy Start Study in the USA was examined for associations between energy expenditure, as determined by self-reported physical activity in early, mid and late pregnancy and infant birth size outcomes (Harrod *et al.*, 2014). Similarly to other studies reported above, early and mid-pregnancy energy expenditure were not associated with infant birth size, while infants of mothers in the highest quartile in late pregnancy had significantly less FM than infants born to mothers in the lowest quartile, with no significant trend observed for FFM or birth weight. Bisson et al. (2017) observed that maternal performance of

VPA in mid or late pregnancy was associated with decreased infant birth weight, while only mid-pregnancy VPA was associated with decreased infant adiposity, as assessed by DEXA. Time spent in moderate physical activity in late pregnancy was positively associated with infant FFM.

2.1.10.5 Maternal lifestyle interventions

Numerous lifestyle interventions aiming to limit GWG, prevent GDM and reduce LGA and macrosomia have been conducted, particularly amongst women with obesity. However, the success of such interventions has been mixed.

A randomised controlled trial (RCT) was conducted amongst women with obesity in Belgium in order to identify whether lifestyle interventions based on a brochure (passive group) or on active education by a nutritionist (active group) could improve dietary habits, increase physical activity and reduce GWG when compared with a control group (Guelinckx *et al.*, 2010). EI did not change for any of the three groups, while physical activity decreased in all groups, particularly during the third trimester. Saturated fat intakes decreased, and protein intakes increased, in both intervention groups, while the opposite change was observed in the control group. However, despite positive dietary changes in both intervention groups, no significant differences in GWG, obstetric or neonatal outcomes were observed between groups.

Infants born to women in the intervention group of an Australian antenatal diet and physical activity RCT were significantly less likely to be classified as macrosomic (birth weight > 4000g) than infants born to women in the control group (Dodd *et al.*, 2014). There were no significant differences in the risk of the infant being born LGA between the two groups, nor were there differences in GWG or other maternal outcomes.

Unlike Guelinckx et al. (2010), the effectiveness of the intervention on dietary intake and exercise in intervention group subjects compared with control subjects was not evaluated.

The UPBEAT RCT in the UK aimed to reduce the incidence of GDM and LGA via a health-trainer lead behavioural intervention (Poston *et al.*, 2015). Although primary outcomes were not significantly different between groups, GWG and maternal sum of skinfolds were significantly lower, and physical activity significantly increased amongst women in the intervention group, compared with those receiving standard antenatal care. Reducing the risk of GDM was also the aim of the Finnish Diabetes Prevention Study (RADIEL) which targeted women with previous GDM and/or obesity (Koivusalo *et al.*, 2016). Women in the intervention arm of the study received individualised lifestyle counselling from dietitians and nurses, as well as free of charge access to swimming pools and exercises classes, while women in the control group received standard antenatal care. Incidence of GDM was significantly reduced in the intervention group compared with controls (13.9 vs 21.6%, $p<0.05$) with GWG also significantly reduced in the intervention group. A similar intervention conducted in Italy also observed a reduction in GDM, LGA, macrosomia, preterm birth and hypertension groups (Bruno *et al.*, 2017). Interestingly, no differences in GWG were observed between groups, and the authors suggest that changes in FM and FFM would have been more appropriate to measure from a metabolic perspective.

The theory of developmental overnutrition was used to inform the development of the ROLO (Randomised Controlled Trial of Low Glycaemic Index Diet in Pregnancy) study in Ireland where women were randomised to receive either a low glycaemic index (GI)

diet or no dietary intervention during their pregnancy. Walsh et al (2012) did not observe any differences between groups for any infant birth size outcomes nor incidence of GDM, but did observe a significant reduction in GWG for women participating in the intervention. Donnelly et al (2014) hypothesised that maternal low GI diet may impact neonatal anthropometry and performed further analysis. Neonates had anthropometric measurements taken within 1-2 days of birth. Infants born to women who participated in the intervention had lower thigh circumference compared to infants born to women in the control, which just reached significance (15.9 ± 1.7cm vs. 16.6 ± 1.5cm, P=0.04). There were no other differences between groups for head, chest, abdominal or mid-upper arm circumferences nor for any skinfold measurements.

Women in the 'Bumps and Beyond' intervention in the UK attended seven sessions with healthy lifestyle midwives, who encouraged women to meet national diet and physical activity recommendations (McGiveron *et al.*, 2015). GWG was significantly lower in the intervention group than the control group (4.5 ± 4.6kg vs. 10.3 ± 4.4kg, $p<0.001$) which was associated with a reduced rate of hypertensive conditions, however, the motivation of women who volunteered for the intervention compared with those who chose not to participate and became the control group is a major limitation. There was no difference in birth weight of infants between groups.

Women with a pre-pregnancy BMI $\geq 35kg/m^2$ were referred for individual dietetic intervention in an Australian pilot study (Robertson and Ladlow, 2017). For multiparous women, the intervention was associated with significantly reduced GWG when compared to previous pregnancies (3.57 ± 5.37 kg vs 14.31 ± 11.23kg, $p<0.001$).

Women who attended three or more sessions gained significantly less weight than those who attended the initial assessment only, which suggests, that for motivated women, individual dietetic assessment can assist in limiting GWG. However, as the number of women of childbearing age with obesity increases, individual dietetic assessment may not be possible to implement within antenatal clinics for all women with obesity.

As shown in the studies discussed above, a recent Cochrane systematic review concluded that interventions comprising diet, exercise or both can reduce the risk of excessive GWG (Muktabhant *et al.*, 2015). Another Cochrane review aimed to review the role of diet and exercise interventions for preventing GDM concluded that moderate quality evidence exists to support their role in reducing the prevalence of GDM (Shepherd *et al.*, 2017). This review also observed reductions in GWG, but no effect on the prevalence of LGA.

2.1.11 **Conclusion from review of the literature**

It is important to gain an understanding of the factors influencing neonatal anthropometric outcomes, as LGA or macrosomic infants with or without excess adiposity at birth have been shown to be at increased risk of adverse consequences such as insulin resistance (Catalano *et al.*, 2009), metabolic syndrome (Boney *et al.*, 2005), type 2 diabetes (Johnsson *et al.*, 2015) and childhood obesity (Schellong *et al.*, 2012). As observed from the current literature, there is consistent evidence to suggest that maternal obesity and excess GWG contribute to increased risk of adverse neonatal anthropometric outcomes (Alberico *et al.*, 2014; Carlsen *et al.*, 2014) as well as longer-term risks (Whitaker, 2004; Mamun, Mannan and Doi, 2014). However,

maternal obesity and GWG are broad outcome measures. The timing and composition of GWG are interesting and under-studied outcome measures that may lead to an increased understanding of the mechanism by which maternal obesity and GWG appear to influence neonatal anthropometric outcomes. Although some studies have examined the relationship between the timing and composition of GWG and infant anthropometrics (Davenport *et al.*, 2013; Kent *et al.*, 2013; Widen *et al.*, 2015; Hivert *et al.*, 2016) there is a lack of studies examining both the timing and composition of GWG at frequent assessments throughout pregnancy, alongside both infant birth weight and infant body composition, particularly in the UK. There is also a lack of recent prospective studies examining these effects according to the most recent IOM recommendations (Rasmussen and Yaktine, 2009).

Maternal diet and physical activity during pregnancy undoubtedly influence GWG and subsequently anthropometric outcomes for offspring. However, despite a wealth of prospective studies linking maternal diet and physical activity to GWG (Stuebe, Oken and Gillman, 2009; Bärebring *et al.*, 2016) and to some extent, infant birth size (Olsen *et al.*, 2007; Knudsen *et al.*, 2013), maternal lifestyle interventions only seem to be successful at reducing GWG (Muktabhant *et al.*, 2015) and not at improving infant birth size outcomes (Shepherd *et al.*, 2017).

In order to develop successful interventions to promote optimal pregnancy outcomes, it is important to understand in more detail how diet, physical activity and the timing and composition of GWG influence infant birth size. The present study will therefore examine the timing and composition of GWG, alongside diet and physical activity at frequent intervals of pregnancy, on neonatal anthropometric outcomes. The study will

be set amongst women with obesity in Plymouth, UK, where rates of obesity amongst women entering pregnancy appear to be high (24.2% in 2017) compared with rates amongst women of childbearing age in the general population in the UK (10-24%; Health and Social Care Information Centre, 2017).

A positivist approach is taken for this research in order to best answer the research questions listed below.

1. **How does diet affect maternal and infant outcomes?**
2. **How does physical activity affect maternal and infant outcomes?**
3. **Does the timing and composition of GWG affect infant birth weight and adiposity?**

Positivist approaches are common within the natural sciences where the aim is to identify associations, and provide the basis for generating laws. Knowledge is arrived at through gathering facts, in this case the measurements of diet, physical activity and changes in maternal weight and body composition, in order to provide a better understanding of the associations between these factors. Within the tradition of positivism, science should be conducted in a way that is free from the researcher's perspectives or beliefs, through the collection of objective data (Bryman, 2012). This study aimed to maximise objectivity using established, validated and replicable measurement procedures which are described in Chapter 3.

2.2 Dietary patterns and gestational weight gain, gestational diabetes and infant macrosomia – a semi-systematic review.

The relationship between diet and health outcomes has traditionally been explored by examining single nutrients or foods which has proved valuable in identifying relationships between dietary intakes of sugar sweetened beverages and incidence of type 2 diabetes (Imamura *et al.*, 2015), dietary fibre and colorectal cancer (Bingham *et al.*, 2003) and saturated fat and coronary heart disease (Ascherio *et al.*, 1996) to name just a few. However, nutrients are not consumed in isolation, and thus examining them in such a way does not account for potential interactive, synergistic, opposition or cumulative effects of multiple nutrients consumed together (Hu, 2002). For example, despite acknowledging an association between diets high in saturated fats and blood cholesterol in their cohort study, Ascherio *et al* (1996) suggested these effects were at least in part mediated by low fibre content of foods containing these nutrients, which paves the way for the study of dietary patterns as opposed to nutrients in isolation. The first papers to examine food patterns and health were published more than 35 years ago (Schwerin *et al.*, 1981). Rather than examining individual nutrients, dietary pattern analysis (DPA) examines the effect of the overall diet on health, giving a broader representation of food intake in the combinations and proportions that it is consumed. It is hypothesised that dietary patterns may provide a more comprehensive approach to understanding how foods consumed in combination, may influence health, and can also aid in the development of translatable dietary advice that can be implemented in free-living populations.

Dietary patterns can be derived theoretically or empirically. Theoretical approaches are *a priori* and hypothesis-driven, based on pre-existing indices of overall dietary quality such as the Healthy Eating Index (HEI), which is based on US Dietary Guidelines for Americans (Kennedy *et al.*, 2017), and Mediterranean Diet (Trichopoulou *et al.*, 1995). These indices are based on pre-existing ideas of what constitutes a 'healthy' diet, which tend to have evolved from studies that examined the impact of single nutrients on health outcomes, which may no longer represent the most rigorous scientific evidence.

Empirically-derived patterns are not based on pre-defined definitions of 'healthy' or 'unhealthy' eating but are instead derived from statistical methods used to generate patterns from dietary data collected from the population of interest (Newby and Tucker, 2004). Factor analysis, principal component analysis (PCA) and cluster analysis are commonly used *a posteriori* approaches to DPA.

Factor analysis and PCA identify dietary patterns based on the degree to which food items or food groups in the dataset are interrelated. A score can then be generated for each pattern and used to examine the relationship between eating patterns and the outcome of interest. Cluster analysis produces sub-groups of individuals with similar dietary patterns which may be based on the frequency, percentage contribution to energy or volume of particular foods or food groups. Once these clusters have been identified, further analysis is necessary to interpret the patterns identified, and to examine differences in health outcomes between groups.

Many studies have examined the role of individual nutrients and foods during pregnancy (Lagiou *et al.*, 2004; Olsen *et al.*, 2007), however, there has been a recent increase in the number of studies examining dietary patterns during pregnancy via dietary indexes (Laraia, Bodnar and Siega-Riz, 2007; Moran *et al.*, 2013) or via empirical methods (Moran *et al.*, 2017). Data from the present cohort study has been examined for associations between individual nutrients and maternal and infant outcomes. In addition, DPA using four-day diet diaries will be conducted to extend the understanding of the combined effects of nutrients and foods consumed during pregnancy. The aim of this semi-systematic review is to review the literature exploring dietary patterns during pregnancy and key outcomes of interest in the present cohort study: GWG, GDM and infant birth size, as well as to explore how DPA may be incorporated into analysis in the study.

2.2.1 **Literature search methods**

An electronic literature search of article titles and abstracts was conducted on PubMed for articles published between 1st January 1981 (when the first papers examining food patterns and health began to emerge) and 14th August 2017. The search terms included the following terms 'dietary patterns' or 'food patterns' or 'diet quality' and 'pregnancy' and returned 331 citations. These citations were screened by title and abstract by one reviewer and 301 were excluded. Studies were only included if they examined dietary patterns during pregnancy and their association with GDM, GWG or infant birth size characteristics. Studies were excluded if they focused on single nutrients or food groups and women with pre-existing medical conditions or illnesses, for example, eating disorders, alcohol or drug dependency or HIV. Full papers were

retrieved for the remaining 32 studies, and 2 additional studies were identified from the reference lists of these studies (Figure 2.2). Of these studies, 27 were included in the review: 5 examined GWG (Table 2.2), 8 looked at GDM (Table 2.3) and 12 focused on infant birth size (Table 2.4). One study reported both GWG and infant birth size as outcomes and another study reported GDM and infant birth size; these studies were reviewed in both relevant sections of the review.

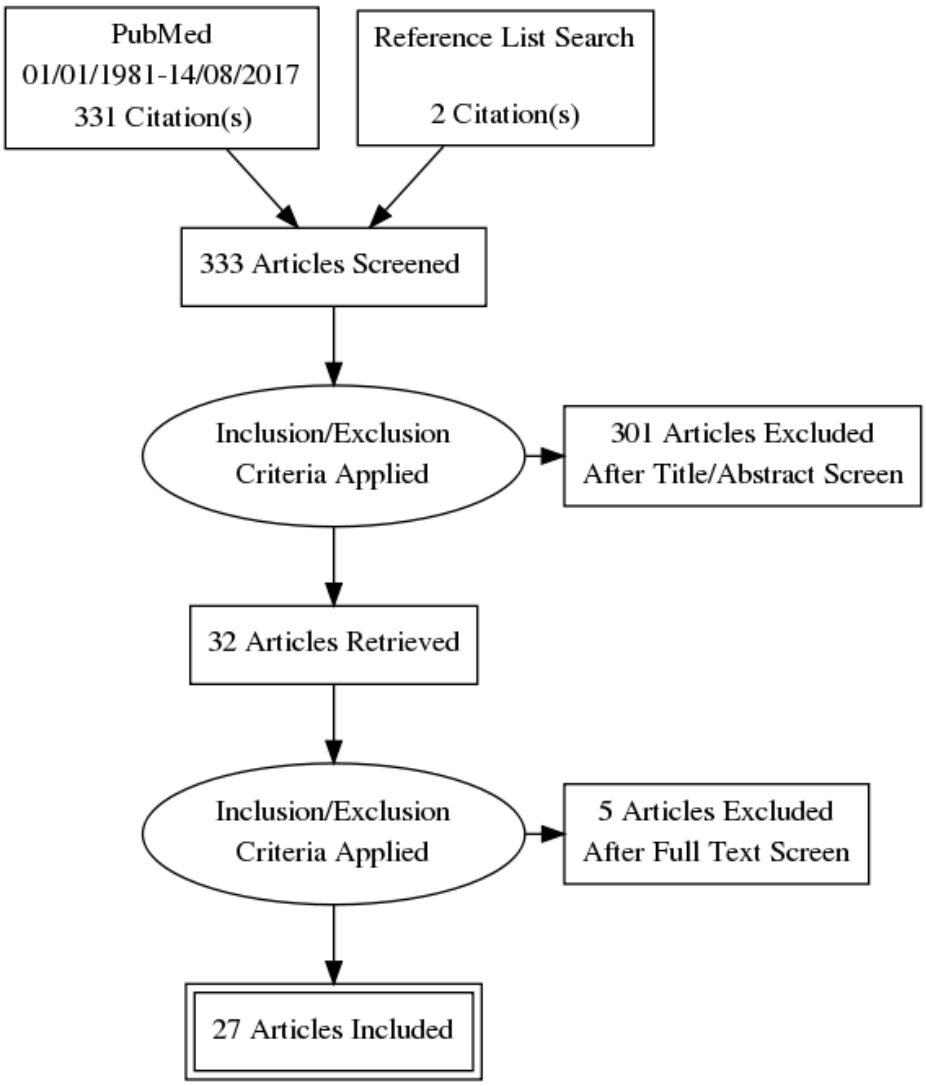


Figure 2.2 Flowchart of study selection

Table 2.2 Dietary patterns and GWG

Study	Study participants (n), country	Dietary pattern assessment method	Patterns identified/index used.	Outcome
Uusitalo *et al.* 2009	3,360, Finland	*A posteriori* – PCA	'Healthy,' 'fast food,' 'traditional bread,' 'traditional meat,' 'coffee,' 'low fat,' and 'alcohol and butter.'	'Fast food' pattern was positively associated, and 'alcohol and butter' pattern inversely associated with rate of GWG.
Hillesund *et al*., 2014	66,597, Norway.	*A priori*-derived.	New Nordic Diet Score (NND).	NND adherence was associated with reduced odds of excess GWG in healthy weight women only.
Shin *et al.,* 2014	490, USA	*A priori*-derived.	Healthy Eating Index of 2005 (HEI-2005).	No association between HEI-2005 and GWG.
Tielemans *et al.*, 2015	3,374, the Netherlands	*A posteriori* – PCA *A priori*-derived.	'Vegetable, oil and fish'; 'Nuts, high-fibre cereals and soy'; and 'Margarine, sugar and snacks.' Dutch Healthy Eating Index.	Adherence to 'margarine, sugar and snacks' associated with excessive GWG.
Shin, Lee and Song., 2016	391, USA	*A posteriori* – factor analysis	'Mixed,' 'healthy,' and 'western.'	Women in the highest tertile of the 'mixed' pattern at higher odds of insufficient GWG, women in the middle tertile at lower odds of excessive GWG.
Wrottesley, Pisa and Norris., 2017.	538, South Africa	*A posteriori* – PCA	'Traditional,' 'western,' and 'mixed.'	'Western,' pattern increased odds (in normal weight women only), and 'traditional,' pattern decreased odds (in total sample and normal weight women) of excessive GWG.

Table 2.3 Dietary patterns and GDM

Study	Study participants (n), country	Dietary pattern assessment method	Patterns identified/index used.	Outcome
Zhang *et al.*, 2006	13,110, USA	*A posteriori* – factor analysis	'Prudent' and 'Western.'	The 'Western' pattern was positively associated and the 'prudent' pattern was inversely associated with GDM incidence.
Radesky *et al.*, 2008	1,733, USA	*A posteriori* – PCA	'Prudent' and 'Western.'	No association between either pattern and GDM.
Tobias *et al.*, 2012	15,254, USA	*A priori*-derived.	Alternate Mediterranean (aMED), Dietary Approaches to Stop Hypertension (DASH) and alternate HEI (aHEI).	All three scores were inversely associated with GDM risk after adjustment for covariates.
Karamanos *et al.*, 2014	1,076, 10 Mediterranean countries.	*A priori*-derived.	Mediterranean Diet Index (MDI).	Incidence of GDM was lower in those with high adherence to MDI.
He *et al.*, 2015	3,063, China	*A posteriori* – PCA	'Vegetable,' 'protein-rich,' 'prudent,' and 'seafood and sweets.'	The 'vegetable' pattern was inversely associated and the 'seafood and snacks' was positively associated with risk of GDM.
Shin, Lee and Song, 2015	253, USA	*A posteriori* – reduced rank regression	'High refined grains, fats, oils and fruit juice,' 'high nuts, seeds, fat and soybean; low milk and cheese,' and 'high added sugar and organ meats; low fruits, vegetables and seafood.'	Women in the highest versus lowest tertiles of all patterns were at significantly higher risk of GDM.

de Seymour *et al.*, 2016	909, Singapore	*A posteriori* – factor analysis	'Vegetable, fruit and rice,' 'seafood-noodle,' and 'pasta, cheese and processed meat.'	The 'seafood-noodle' pattern was associated with significantly lower incidence of GDM.
Flynn *et al.*, 2016	1,023, UK	*A posteriori* – factor analysis	'Fruit and vegetables,' 'African/Caribbean,' 'processed,' and 'snacks,'	'African/Caribbean' and 'snacks' patterns were significantly associated with incidence of GDM.
Tryggvadottir *et al.*, 2016	168, Iceland	*A posteriori* – PCA	'Prudent'	Adherence to 'prudent' pattern associated with reduced risk of GDM.

Table 2.4 Dietary patterns and infant birth size outcomes.

Study	Study participants (n), country	Dietary pattern assessment method	Patterns identified/index used.	Outcome
Thompson *et al.*, 2010	1,714, New Zealand	*A posteriori* – PCA	'Traditional,' 'junk,' and 'fusion.'	Adherence to the 'traditional' pattern reduced the odds of SGA.
Rodríguez-Bernal *et al.*, 2010	787, Spain	*A priori*-derived.	AHEI.	HEI score positively associated with birth weight and length and reduced risk of SGA.
Okubo *et al.*, 2012	803, Japan	*A posteriori* – cluster analysis	'Meat and eggs,' 'wheat products,' and 'rice, fish and vegetables.'	Birth weight was significantly lower (compared to the two other groups), and odds of SGA significantly higher (compared to the 'rice, fish and vegetables' group), in women adhering to the 'wheat products' pattern.
Knudsen *et al.*, 2013	44,612, Denmark	*A posteriori* – PCA	'Western' and 'health conscious.'	Adherence to the 'Western' pattern was associated with higher risk of SGA baby compared with the 'health conscious' pattern.
Poon *et al.*, 2013	893, USA	*A priori*-derived.	AHEI for pregnancy (AHEI-P).	No association between dietary patterns and risk of SGA or LGA.
Hillesund *et al.*, 2014	66,597, Norway.	*A priori*-derived.	New Nordic Diet Score (NND).	High NND adherence was associated with reduced odds of SGA and increased odds of LGA.

Coelho *et al.*, 2015	1,298, Brazil	*A posteriori* – PCA	'Prudent,' 'traditional,' 'Western,' and 'snack.'	'Snack' pattern in the third trimester was significantly associated with birth weight in pregnant women <20 years old only, with no associations observed for other patterns in this group or in women aged ≥20 years.
Colón-Ramos *et al.*, 2015	1,151, USA	*A posteriori* – PCA	'Healthy,' 'healthy-Southern,' 'Southern,' 'mixed,' 'healthy-processed,' 'processed-Southern,' 'processed.'	No association with dietary patterns and birth size outcomes.
Chia *et al.*, 2016	923, Singapore	*A posteriori* – PCA	'Vegetable, fruit and rice,' 'seafood-noodle,' and 'pasta, cheese and processed meat.'	Greater adherence to the 'vegetable, fruit and rice,' pattern was associated with higher ponderal index and increased risk of LGA.
Flynn *et al.*, 2016	1,023, UK	*A posteriori* – factor analysis	'Fruit and vegetables,' 'African/Caribbean,' 'processed,' and 'snacks,'	No association between dietary patterns and risk of SGA and LGA.
Lu *et al.*, 2016	6,954, China	*A posteriori* – cluster analysis	'Cereals, eggs and Cantonese soups,' 'dairy,' 'fruits, nuts and Cantonese desserts,' 'meats,' 'vegetables,'	'Fruit, nuts and Cantonese desserts,' and 'varied' patterns had significantly heavier infants than women consuming a 'cereals, eggs and Cantonese soups' pattern,' who also had higher odds of SGA infant than those consuming a 'varied' pattern.

Martin *et al.*, 2016	389, USA	*A posteriori* – latent class analysis	'Fruit, vegetables, refined grains, red and processed meats, pizza, French fries, sweets, salty snacks and soft drinks,' 'fruits, vegetables, baked chicken, whole-wheat bread, low-fat dairy and water,' and 'white bread, red and processed meats, fried chicken, French fries and vitamin-C rich drinks.'	The 'white bread, red and processed meats, fried chicken, French fries and vitamin-C rich drinks,' pattern was inversely associated with BMI-for-age z score.
Shapiro *et al.*, 2016	1,079, USA	*A priori*-derived.	HEI – 2010.	HEI_2010 score ≤57 was associated with higher infant FM and percentage FM.
Starling *et al.*, 2017	764, USA	*A posteriori* – reduced rank regression.	'Poultry, nuts, cheese, fruits, wholegrains, added sugars and solid fats,' and 'Eggs, starchy vegetables, solid fats, fruits, refined grains; low dairy, dark-	'Poultry, nuts, cheese, fruits, wholegrains, added sugars and solid fats,' was positively associated with newborn FFM, while 'eggs, starchy vegetables, solid fats, fruits, refined grains; low dairy, dark-green vegetables and whole grains,' was

	green vegetables and whole grains.’	positively associated with birth weight, FM and adiposity.

2.2.2 **Dietary patterns and gestational weight gain**

Excessive GWG during pregnancy has been shown to be associated with adverse outcomes for both mother and infant, including increasing the risk of GDM (Hedderson, Gunderson and Ferrara, 2010), hypertensive disorders (Macdonald-Wallis *et al.*, 2013), foetal macrosomia (Rodrigues *et al.*, 2010) and emergency delivery (Li, Liu and Zhang, 2015). Table 2.2 summarises the findings of studies which have examined the association between dietary patterns and GWG.

A population-based prospective cohort study in The Netherlands compared *a posteriori*-derived and *a priori*-defined dietary patterns assessed using a FFQ with GWG assessed at three time points in 3374 pregnant women (Tielemans *et al.*, 2015). PCA was used to identify three dietary patterns while the *a priori*-derived pattern was based on the Dutch Healthy Eating Index. Adherence to these patterns was examined for associations with GWG during early-, mid- and late-pregnancy, as well as total GWG and adequacy of GWG according to IOM guidelines (Rasmussen and Yaktine, 2009). A 'vegetable, oil and fish' pattern was found to be associated with higher early-pregnancy GWG for normal weight women in the highest quartile versus the lowest quartile. Odds of excessive GWG was greatest in women with highest adherence to a 'margarine, sugar and snacks' pattern, while the *a priori*-derived pattern was not associated with GWG at all. Adherence to the New Nordic Diet (NND), another *a priori*-defined score was associated with significantly lower odds of GWG in excess of IOM guidelines for healthy weight women in Norway, while there was no significant association between NND adherence and GWG category for women classified as

overweight or obese (Hillesund *et al.*, 2014). 24 hour recall data from the US National Health and Nutrition Examination Survey (NHANES) 2003-2006 was used to assess whether adherence to the HEI-2005 was associated with GWG according to IOM guidelines at different stages of pregnancy in a sample of 490 pregnant women (Shin *et al.*, 2014). HEI scores did not significantly differ between women gaining below, within or in excess of IOM GWG guidelines after adjustment for co-variates. A similar study was conducted by the authors using the same data for 391 women from NHANES 2003-2006, but using *a posteriori*-derived dietary patterns obtained using factor analysis (Shin, Lee and Song, 2016). 'Mixed,' 'healthy,' and 'western,' dietary patterns were identified. Only the 'mixed' pattern appeared to be associated with GWG, with women in the highest tertile exhibiting significantly greater odds of GWG below IOM guidelines compared with those in the lowest tertile, and women in the middle tertile exhibiting significantly lower odds of GWG above IOM guidelines, compared with those in the lowest tertile.

PCA was used to identify dietary patterns from FFQ data in a Finnish Cohort study of 3360 women (Uusitalo *et al.*, 2009). Seven dietary patterns were identified, and of these, the 'fast food' and 'alcohol and butter' patterns were positively and inversely associated with GWG rate, respectively in a dose-dependent manner. A similar study was conducted in black South African women from early-pregnancy FFQ data via PCA (Wrottesley, Pisa and Norris, 2017). A 'mixed' pattern showed a significant positive association with GWG for all women, but when split by BMI category, this association only remained significant for women with obesity, not normal or overweight women. A

'traditional' pattern showed decreased odds of excessive GWG for the total sample and normal weight women. Adherence to the 'western' pattern increased the odds of excessive GWG in women with a healthy BMI only, but after adjustment for covariates, this association no longer remained significant. These studies that used PCA to identify associations between dietary patterns and GWG suggest that specific dietary patterns may play a role in GWG, however, a consistent role of these patterns in GWG across pregnancy and BMI categories is yet to be identified. With the development of BMI-specific GWG guidelines from the IOM, it is important that dietary advice is specific and relevant for women belonging to all BMI classes. To our knowledge, no studies have examined the association between dietary patterns and changes in maternal body composition during pregnancy which is another important component of GWG which requires further exploration alongside dietary patterns.

2.2.3 **Dietary patterns and GDM**

GDM is associated with elevated risk of adverse outcomes for both mother and infant (Jovanovic and Pettitt, 2001) with prevalence increasing with maternal obesity (Sathyapalan, Mellor and Atkin, 2010). Table 2.3 summarises the findings of studies which have examined the association between dietary patterns and GDM.

A prospective cohort study which included 13,110 women from the Nurses' Health Study II identified two dietary patterns from FFQ data by factor analysis and examined their association with risk of GDM (Zhang *et al.*, 2006). After adjustment for potential confounders, women in the highest quintile of the 'western' pattern, were at significantly higher risk of GDM than women in the lowest quintile. Conversely, those

in the highest quintile of a 'prudent' pattern were at significantly lower risk of GDM. Another prospective pregnancy and birth cohort study which examined FFQ data from 1,733 women enrolled in Project Viva in the US (Radesky *et al.*, 2008) calculated 'western' and 'prudent' dietary pattern scores to facilitate comparison with Zhang and colleagues (2006) but did not observe any association between either pattern and glucose tolerance or GDM incidence. Studies varied in design, although FFQ items were similar, data was collected as much as four years prior to GDM diagnosis in the Nurses' Health Study II (Zhang *et al.*, 2006), while the FFQ in Project Viva was administered during early pregnancy and asked about dietary habits since their last menstrual period.

In Iceland, a prospective observational study of 168 women used PCA to extract dietary patterns from a 4-day weighed record collected mid-pregnancy (Tryggvadottir *et al.*, 2016). One dietary pattern was identified and labelled as 'prudent'. Adherence to this pattern was associated with significantly lower risk of GDM after adjustment, and a similar association was observed when only women classified as overweight or obese were included in analysis. Three dietary patterns were identified by reduced rank regression from 24 hour recall data from 253 US women participating in the NHANES 2003-2012: 'high refined grains, fats, oils and fruit juice,' 'high nuts, seeds, fat and soybean; low milk and cheese,' and 'high added sugar and organ meats; low fruits, vegetables and seafood'(Shin, Lee and Song, 2015). Women in the highest versus lowest tertiles of all patterns were at significantly higher risk of GDM, however, this

study was limited by the fact that the point of gestation at which dietary data was collected varied considerably between participants.

The UPBEAT randomised controlled trial in the UK aimed to investigate the effect of a diet and physical activity intervention on dietary patterns over the course of pregnancy in pregnant women with obesity and explored associations of dietary patterns with GDM incidence in the combined control/intervention cohort of 857 women (Flynn *et al.*, 2016). Four dietary patterns were derived from FFQ data using factor analysis: 'fruit and vegetables,' 'African/Caribbean,' 'processed,' and 'snacks,' and in an adjusted model, women in the highest quartiles of both the 'processed' and 'African/Caribbean' patterns were significantly more likely to develop GDM than those in the lowest quartiles.

The Growing Up in Singapore Towards Healthy Outcomes (GUSTO) study – a multi-ethnic Asian cohort set in Singapore identified three dietary patterns via factor analysis from mid-pregnancy 24 hour recall data for 909 pregnant women: 'vegetable, fruit and rice,' 'seafood-noodle,' and 'pasta, cheese, processed and meat' (de Seymour *et al.*, 2016). After adjustment for covariates, the 'seafood-noodle' pattern was associated with significantly lower incidence of GDM, while the other patterns showed no association with GDM after adjustment. The authors of this study point out that the 'seafood-noodle' pattern associated with GDM in this study is substantially different to the patterns found to be associated with GDM in western populations, which suggests that advice derived from studies examining dietary patterns and GDM should be specific to the culture and ethnicity of the population.

A prospective cohort study conducted in 3063 Chinese women identified four dietary patterns from FFQ data by PCA (He *et al.*, 2015). The lowest tertile of the 'vegetable' pattern and highest tertile of the 'sweets and seafood' pattern were associated with the highest incidence of GDM, while the 'prudent' and 'protein-rich' patterns were not associated with GDM incidence. The results of this study slightly contradict those found in the Singaporean study (de Seymour *et al.*, 2016) where the pattern characterised by high seafood (and noodle) intake was associated with lower incidence of GDM amongst a cohort where a majority of women identified as Chinese.

Two studies examined *a priori*-defined dietary pattern scores and GDM. A prospective study which included 1076 pregnant women from 10 Mediterranean countries examined the relationship between adherence to the Mediterranean Diet Index (MDI) pattern and GDM incidence (Karamanos *et al.*, 2014). Women who developed GDM had significantly lower MDI adherence than women who did not, while incidence of GDM was lower in those with higher adherence. Another study that used data from 15,254 participants in the Nurses' Health Study II cohort also examined adherence to the Mediterranean Diet using the alternate Mediterranean diet score (a-MED), alongside Dietary Approaches to Stop Hypertension (DASH) and alternate-HEI scores (Tobias *et al.*, 2012). Women in the highest quartiles of adherence to a-MED, DASH and a-HEI had a 24%, 34% and 46% lower incidence of GDM, respectively, when compared with women in the lowest quartiles, suggesting that adherence to 'healthy' dietary patterns reduces the risk of GDM.

Of the studies that observed associations between *a posteriori*-derived dietary patterns in Western populations, 'prudent' dietary patterns high in fruits, vegetables and fish appear to be protective against GDM, while dietary patterns characterised by low intakes of fruit and vegetables, and high intakes of added sugars and processed foods appear to increase risk of GDM. Similar dietary patterns are promoted in the diet scores studied in the studies that examined *a priori*-defined scores, suggesting that at least for Western populations, antenatal advice should continue to promote adherence to these types of diet. Optimal dietary patterns for the reduction of risk of GDM amongst Asian cohorts is less clear, highlighting the need for dietary patterns studies specific to target populations.

2.2.4 **Dietary patterns and infant birth size**

Infant birth size, including birth weight and adiposity are key determinants of infant health. Both foetal macrosomia, usually defined as a birth weight ≥4kg or 4.5kg, and LBW, usually defined as birth weight <2.5kg, are associated with increased risk of complications during delivery (Bérard *et al.*, 1998; Doctor *et al.*, 2001), as well as increased risk of obesity and metabolic syndrome in later life (Whitaker, 2004; Boney *et al.*, 2005). It is therefore important to understand how dietary patterns during pregnancy may influence infant birth size outcomes (Table 2.4).

Two studies have used multiple 24 hour recall data collected across pregnancy from the Healthy Start prospective cohort study conducted in the USA. The first found that lower adherence to the *a priori*-defined HEI-2010 score was significantly associated with neonatal FM, but not FFM or birth weight in 1079 mother-offspring pairs (Shapiro

et al., 2016). The second identified two dietary patterns via reduced rank regression in 764 mother-infant pairs (Starling *et al.*, 2017). Infant FFM was significantly higher in women in the highest tertile of a pattern characterised by high intakes of poultry, nuts, cheese, fruits, wholegrains, added sugars and solid fats compared with women in the lowest tertile, with no differences in FM or birth weight; while those in the highest tertile of a pattern characterised by higher consumptions of eggs, starchy vegetables, solid fats, fruits, refined grains and lower intakes of dairy, dark-green vegetables and whole grains, had infants with significantly higher birth weight and FM, while FFM was not affected.

There was no association between dietary patterns and incidence of LGA, SGA or macrosomia in the UPBEAT study, which showed an association with GDM as discussed earlier in the manuscript (Flynn *et al.*, 2016). A separate study looking at the same *a posteriori*-derived dietary patterns in the GUSTO study as reported for GDM (de Seymour *et al.*, 2016) also examined infant birth size outcomes (Chia *et al.*, 2016). In this study, the 'vegetable, fruit and rice' pattern was associated with significantly higher ponderal index and risk of LGA birth, with no associations with birth weight, birth length or SGA, nor any association with either of the other dietary patterns. High, as compared with low adherence to the NND score, which was associated with lower odds of excessive GWG as previously discussed, was also associated with reduced odds of SGA, and higher odds of LGA birth (Hillesund *et al.*, 2014).

Two studies examined the relationship between *a priori*-defined diet scores and infant birth size. A Spanish cohort of 787 women observed a positive association between

diet quality, as assessed by adherence to the a-HEI in the first trimester, and adjusted birth weight and length, with women in the highest quintiles at lowest risk of delivering a SGA infant (Rodríguez-Bernal *et al.*, 2010). These findings differ from those in the US Healthy Start cohort, which did not observe an association between HEI score and birth weight (Shapiro *et al.*, 2016). A US cohort of 893 women enrolled in the Infant Feeding Practices Study II also assessed diet quality by adherence to a-HEI, as well as a-MED and carbohydrate quality, in the third trimester (Poon *et al.*, 2013), with no dietary pattern associated with birth weight, LGA or SGA.

A US prospective cohort study examined dietary patterns derived from a mid-pregnancy FFQ in 389 mother-child pairs (Martin *et al.*, 2016). Three dietary patterns were identified, pattern 1: 'fruit, vegetables, refined grains, red and processed meats, pizza, French fries, sweets, salty snacks and soft drinks,' pattern 2: fruits, vegetables, baked chicken, whole-wheat bread, low-fat dairy and water,' and pattern 3: 'white bread, red and processed meats, fried chicken, French fries and vitamin-C rich drinks.' After adjustment, an inverse association between pattern 3 and BMI-for-age z score at birth was identified, with no associations observed for the other patterns. Another prospective cohort study of 1151 women, this time set in Southern US, did not observe associations between dietary patterns and birth size outcomes (Colón-Ramos *et al.*, 2015). A Brazilian longitudinal study found that a 'snack' pattern in the third trimester was significantly associated with birth weight in pregnant women <20 years old only, with no associations observed for 'prudent,' 'traditional,' or 'western' patterns in this group or in women aged ≥20 years (Coelho *et al.*, 2015).

Six dietary patterns were identified from FFQ data from mid-pregnancy using cluster analysis in a large prospective cohort study of 6954 women in China (Lu *et al.*, 2016). Women whose diets were characterised by a 'fruit, nuts and Cantonese desserts,' or 'varied' pattern had significantly heavier infants than women consuming a 'cereals, eggs and Cantonese soups' pattern,' who also had higher odds of SGA infant than those consuming a 'varied' pattern after adjustment for confounders. 'Meat and eggs,' 'wheat products,' and 'rice, fish and vegetables,' patterns were identified from FFQ data for 803 Japanese women (Okubo *et al.*, 2012). After adjustment for confounders, women in the 'wheat products' pattern had infants with significantly lower birth weight than women in both other patterns, and significantly higher odds of SGA infant than women in the 'rice, fish and vegetables,' pattern, suggesting that a diet high in bread, confectionary and soft drinks increases the risk of LBW. A case-control study in New Zealand observed a significant effect of a 'traditional' dietary pattern in early, but not late pregnancy, on reducing the risk of SGA, with no significant effect of 'junk' or 'fusion' dietary patterns on SGA at either time-point (Thompson *et al.*, 2010). Findings from a Danish study examining mid-pregnancy FFQ data from women enrolled in the Danish National Birth Cohort identified that a diet based on 'red and processed meat and high fat dairy,' labelled as a 'Western' pattern was associated with increased risk of SGA compared with women consuming a 'Health Conscious' pattern characterised by higher intake of vegetables, fruits, poultry and fish (Knudsen *et al.*, 2013).

It is difficult to make comparisons between studies examining dietary patterns and infant birth size outcomes as not only is there variation in the types of patterns identified, but birth size outcomes reported also differ between studies with some reporting adiposity as FM and FFM, others looking at birth weight, and other reporting SGA or LGA outcomes.

Adherence to *a priori*-defined diet quality scores such as a-HEI and NND in early pregnancy appears to reduce the risk of SGA (Rodríguez-Bernal *et al.*, 2010; Hillesund *et al.*, 2014), while one study observed a decrease in FM (Shapiro *et al.*, 2016). Findings from studies exploring *a posteriori*-derived dietary patterns were mixed, with some studies observing that typically 'western' patterns high in refined grains, fat, and red and processed meats, were associated with adverse birth size outcomes such as high birth weight, FM or SGA (Okubo *et al.*, 2012; Knudsen *et al.*, 2013; Martin *et al.*, 2016; Starling *et al.*, 2017); while other studies observed no associations with such patterns (Coelho *et al.*, 2015; Colón-Ramos *et al.*, 2015; Flynn *et al.*, 2016; Martin *et al.*, 2016). Some studies also showed that adherence to 'traditional' or 'healthy' patterns appeared to improve birth size outcomes such as reducing the risk of SGA (Thompson *et al.*, 2010; Knudsen *et al.*, 2013) and increasing FFM (Starling *et al.*, 2017). With the exception of one study (Chia *et al.*, 2016), following traditional 'healthy eating' guidelines and consuming foods such as vegetables, fruits, poultry, fish and dairy was not associated with any adverse birth size outcomes.

2.2.5 **Discussion**

This review has identified many research studies that have examined dietary patterns during pregnancy and their potential associations with GWG, GDM and infant birth size, however, due to methodological and study population differences, it is difficult to draw any firm conclusions.

In general, adherence to *a priori*-defined diet scores tended to improve outcomes for GDM (Tobias *et al.*, 2012; Karamanos *et al.*, 2014) and infant birth size (Rodríguez-Bernal *et al.*, 2010; Hillesund *et al.*, 2014; Shapiro *et al.*, 2016), but did not consistently appear to influence GWG (Shin *et al.*, 2014; Tielemans *et al.*, 2015), with the exception of one study (Hillesund *et al.*, 2014). Similarly, 'traditionally healthy' *a posteriori*-derived dietary patterns high in fruits, vegetables, wholegrains, fish and poultry tended to be associated with optimal GWG (Wrottesley, Pisa and Norris, 2017), GDM (Zhang *et al.*, 2006; Tryggvadottir *et al.*, 2016) and infant birth size outcomes (Thompson *et al.*, 2010; Knudsen *et al.*, 2013; Starling *et al.*, 2017) while a diet characterised by high processed meats, fried foods, added sugar and high fat dairy appears to increase risk of excessive GWG (Uusitalo *et al.*, 2009; Tielemans *et al.*, 2015; Wrottesley, Pisa and Norris, 2017), GDM (Zhang *et al.*, 2006; Flynn *et al.*, 2016) and infant birth size (Martin *et al.*, 2016; Starling *et al.*, 2017).

Dietary patterns derived from data obtained in early to mid-pregnancy tended to be more successful at identifying associations between diet and maternal and infant outcomes (Rodríguez-Bernal *et al.*, 2010; Hillesund *et al.*, 2014; Tielemans *et al.*, 2015; de Seymour *et al.*, 2016; Flynn *et al.*, 2016; Lu *et al.*, 2016; Shin, Lee and Song, 2016;

Tryggvadottir *et al.*, 2016; Wrottesley, Pisa and Norris, 2017) than those that relied on data collected later in pregnancy (Thompson *et al.*, 2010; Poon *et al.*, 2013; Coelho *et al.*, 2015). Future studies should therefore ensure that dietary data is collected early in pregnancy, while intervention studies should commence soon after conception in order to maximise the opportunity to influence outcomes.

Methods used for deriving *a posteriori* dietary patterns varied considerably between studies with the majority employing PCA, and others using factor analysis, cluster analysis and reduced rank regression. The methods employed for the collection of dietary data from participants also varied between studies with the majority using FFQs and a minority using 24 hour recall or food diaries. Dietary patterns derived from PCA of FFQs and diaries (Crozier *et al.*, 2008) and FFQs and 24 hour recalls (Loy and Jan Mohamed, 2013) obtained from pregnant women have shown reasonable agreement. Methodological differences, as well as the differences in the number and types of dietary patterns derived from each cohort, once again make comparison difficult particularly as the foods consumed varied considerably across the populations studied. Dietary advice should therefore only be based on evidence from studies conducted in the population of interest, and future research is required across all cultures in order to derive good quality evidence surrounding optimal dietary patterns during pregnancy.

It is also important to note that the current review is limited by its semi-systematic nature. Where possible, PRSIMA guidance was followed to ensure that the process was documented, repeatable and not missing key studies in the field (Shamsee*r et al*,

2015), however, the review was not truly systematic as only one reviewer was available to screen articles, and only one database was searched. It is therefore entirely possible, and likely that relevant studies have not been included in this review, and this should be considered a limitation.

With regards to the present study, it is important to gain insight into dietary patterns within the present small group of Caucasian women with obesity; recruited from antenatal clinic in Plymouth, UK. PCA will be used to explore the combinations of foods commonly consumed within this population, rather than using cluster analysis, which is more useful for gaining insight into patterns within subgroups of a population (Ocké, 2013). Dietary data is available for women from approximately weeks 12, 28 and 36 gestation. However, 25% of the present, small cohort were diagnosed with GDM at approximately week 28 of their pregnancy, so may have changed their diet before, during or after their diagnosis in response to a positive oral glucose tolerance test (OGTT) thus influencing their food diary at week 28. Therefore, only dietary patterns from the first trimester were reported and examined for associations with maternal and infant outcomes in the present cohort study in order to avoid excluding women who developed GDM. As discussed previously, studies that examined dietary patterns early, rather than later in pregnancy also tended to be more likely to be associated with maternal and infant outcomes.

In conclusion, diets high in fruits, vegetables, wholegrains, fish and poultry and low in refined grains, added sugars and red and processed meats tended to be associated with the best GWG, GDM and birth size outcomes. However, the methods, time-points

and populations on which dietary patterns was assessed varied considerably, and further research is required in order to elucidate optimal dietary advice for pregnant women at risk of these outcomes. The gaps in the current literature, along with the data from the present observational cohort study, provide a unique opportunity to explore dietary patterns and their association with GWG, GDM and birth size outcomes in pregnant women with obesity.

Chapter 3 **Methodology**

3.1 Recruitment of participants

Ethical approval was obtained from the NHS Health Research Authority National Research Ethics Service (London – Central, REC reference number: 14/LO/1660; Appendix 1) and local Research and Development (R&D) approval was obtained from Plymouth Hospitals NHS Trust (PHNT) (R&D reference number: 14/P/134; Appendix 2). Women were recruited from Derriford Hospital antenatal clinic in Plymouth, UK between January 2015 and November 2016.

Potential participants were identified by a research midwife from PHNT and eligible women meeting inclusion criteria were approached at their dating scan appointment by the researcher and given an information sheet to read while waiting (Appendix 3). Interested women were then signposted back to the researcher after their scan by their sonographer to make a provisional first appointment with the researcher at least 3 days in the future. This gave potential participants plenty of time to consider their participation in the study and to ask any questions prior to giving consent.

3.1.1 **Inclusion criteria**

Women aged between 18 and 40 years, with a BMI ≥ 30 and <40 kg/m^2 at booking and pregnant with a singleton pregnancy were eligible to take part in the study. For ethical reasons, women younger than 18 years were not approached, and as advancing maternal age tends to be associated with increased risk of adverse outcomes such as pre-eclampsia, gestational diabetes, macrosomia and LBW (Cleary-Goldman *et al.*, 2005; Montan, 2007), women aged greater than 40 years were also excluded. The aim

of the study was to examine GWG patterns and pregnancy outcomes amongst women with obesity. Women were approached if their booking BMI was greater than or equal to 30 kg/m^2 but less than 40 kg/m^2 as maternal BMI greater than this has been shown to be associated with increased risk of adverse outcomes (Scott-Pillai *et al.*, 2013), and the present study was not adequately powered to detect differences between BMI categories.

The present study required maternal anthropometric, diet and physical activity data to be collected as close as possible to the end of the first trimester of pregnancy. Therefore, only women whose pregnancies were dated at ≤13 weeks were invited to participate in order to take consent and collect data at ≤14 weeks gestation. Women with multiple pregnancies were also excluded as patterns of GWG and foetal growth differ from women experiencing a singleton pregnancy (Rasmussen and Yaktine, 2009).

3.1.2 **Exclusion criteria**

Pre-existing diabetes mellitus prior to pregnancy has been shown to increase the risk of numerous maternal and perinatal complications, including macrosomia (Evers, Valk and Visser, 2004). Women with pre-existing type I or type II diabetes mellitus were therefore not eligible to take part in the study.

Previous studies have noted differences in the patterns of GWG (Savitz *et al.*, 2011) and neonatal anthropometric outcomes (Deierlein *et al.*, 2011) between different ethnic groups. The present study was carried out within Plymouth, in the South West of England where the population is primarily White Caucasian, with 95.4% identifying themselves as belonging to this group (Office for National Statistics, 2013). Only

women who described their ethnicity as White Caucasian were therefore eligible to participate in the study, as it would not have been possible to observe differences between ethnic groups, while maintaining power in our sample size.

3.2 Calculation of sample size

Based on previous literature that examined the association between birth weight and GWG and observed effect sizes of 0.29 and 0.4, respectively, (Vesco *et al.*, 2011; Badon, Dyer and Josefson, 2014), the following sample size calculations were performed to give a significance level of 0.05 and power of 0.80, (Table 3.1). We aimed to detect a medium effect size of 0.3 and therefore to recruit a total of 97 participants - 82 plus 14 to allow for up to 15% dropout as observed in similar studies in the UK that placed similar burden on women during their pregnancy (Poston *et al.*, 2015; Narayanan *et al.*, 2016).

Table 3.1 Sample size calculations

Effect size	**Sample size**
0.1 (small)	779
0.15	343
0.20	191
0.25	120
0.30 (medium)	82

3.3 Data collection during pregnancy

Following recruitment, participants were visited by the researcher who obtained both verbal and written consent (Appendix 4), followed by a first set of anthropometric measurements. This was followed by four days of diet and physical activity data

collection. The first visit tended to occur between 12 and 14 weeks gestation. Further visits occurred at the end of the second trimester at approximately week 28 of gestation, and at the end of the third trimester at approximately week 36 of gestation. These subsequent visits also involved the collection of anthropometric data and were also followed by a four day period of diet and physical activity data collection.

3.4 Maternal Outcomes

3.4.1 **Maternal baseline information**

A questionnaire was administered to the participant at the first visit, with questions concerning age, parity, occupation, folic acid use, smoking, alcohol and the participant's experience of pregnancy sickness (Appendix 5). The participant's postcode at the time of enrolment was used to identify their lower-layer super output area (LSOA) and thus the Index of Multiple Deprivation for their area using UK 2011 Census data (Department for Communities and Local Government, 2015). The Index of Multiple Deprivation is based on 37 separate indictor of deprivation and every LSOA is ranked according to its level of deprivation from the most deprived area (1^{st}) to the least deprived area (32844^{th}). For each participant, the Multiple Index of Deprivation rank and decile is reported.

3.4.2 **Anthropometric outcomes**

Maternal pre-pregnancy BMI was calculated as weight in kg divided by height in metres squared using height and weight measurements taken at booking (<12 weeks gestation) by the participant's midwife. Gilmore and Redman (2014) dispute the use of early pregnancy weight to calculate BMI, and observed misclassification rate of up to

10%. However, booking BMI calculated in this way was the only means of identifying eligible participants prior to recruitment at week 12 of gestation. All participants had a BMI 30-40 kg/m^2 and so BMI was further categorised according to WHO classification (World Health Orgnanisation, 1995) as obese class I (BMI ≥ 30 and <35 kg/m^2) or obese class II (BMI ≥ 35 and < 40 kg/m^2).

In order to reduce inter-midwife and inter–equipment variability, height was measured by the researcher at the first visit using a portable stadiometer (Seca 213, Hamburg, Germany) according to the 'stretch stature' protocol described by the International Society for the Advanacement of Kinanthropometry (ISAK) (Stewart *et al.*, 2011). Participants removed their shoes and stood underneath the headplate with their back and heels against the rod, feet flat and together and with their arms hanging loose at their sides. The participant's head was moved so that the Frankfurt Plane was in a horizontal position. The researcher applied gentle upward lift through the mastoid process, and lowered the headplate, compressing the hair as much as possible. The participant stepped away from the stadiometer, and the researcher ensured the headplate remained stationary. Height could then be recorded to the nearest millimetre.

Maternal body weight is routinely recorded by a midwife at the initial antenatal booking appointment only. In order to examine GWG throughout pregnancy, weight was measured at each visit at the end of each trimester using the same digital scales for each participant throughout the study's duration (Seca 888, Hamburg, Germany). Participants removed shoes, heavy outer garments, heavy jewellery and anything

heavy from pockets (e.g. keys, loose change etc.). Scales were tared before the subject stepped onto the scales with weight evenly spread between two feet. Weight was recorded to the nearest 0.1 kg.

3.4.3 **Gestational weight gain**

GWG was recorded as a simple difference between weight at each study visit to give a crude value for GWG in each trimester and a 'total' GWG for the study duration. There are several limitations associated with reporting GWG in this way, particularly as participants in our study were not recruited until the twelfth week of gestation, we were unable to obtain a pre-pregnancy weight, which is critical for determining total GWG that is comparable with IOM recommendations (Rasmussen and Yaktine, 2009) and observations in other literature.

Although studies have shown a high level of agreement between self-reported pre-pregnancy weight and clinical records (Phelan *et al.*, 2011), increased under-reporting has been observed amongst women with overweight or obesity (Thomas *et al.*, 2014) and many women in the current study did not know their pre-pregnancy weight. Other studies have suggested early first trimester weight as a valid proxy for pre-pregnancy weight (Krukowski *et al.*, 2016) although this has been disputed as mentioned previously (Gilmore and Redman, 2014). Therefore, although available, booking weight has not been considered a suitable proxy to estimate total GWG due to variations in gestation at booking and the availability of calibrated scales in booking clinics.

Total GWG may also not account for the potential opportunity for further weight gain between the final study visit at approximately week 36, and delivery (up to 6 weeks later). Failure to adjust GWG for gestation has been shown to overestimate adherence to IOM guidelines. Gilmore and Redman (2014) demonstrated that by adjusting for the length of gestation, the number of women defined as exceeding IOM guidelines for GWG increased by 40%.

In the present study, the timing of GWG as well as total GWG in relation to the IOM guidelines was of particular interest. The IOM guidelines, displayed in Table 3.2, provide weekly incremental GWG guidelines for the second and third trimesters specific to pre-pregnancy BMI, as well as total GWG guidelines, in which a first trimester weight gain of 0.5-2kg is assumed (Rasmussen and Yaktine, 2009). Rate of total GWG over the study duration, as well as rate of GWG in the second and third trimesters has been calculated to adjust for gestation for each participant. Participants were further classified as achieving 'insufficient', 'optimal' or 'excessive' GWG according to their rate of GWG at each of these time points according to IOM ranges on GWG.

For example, GWG of 8.0 kg between week 12 and 28 would have been classified as 'excessive' as the rate of GWG would be 0.5 kg/week, which is greater than the recommended range of 0.17-0.27 kg/week

Table 3.2 Recommendations for total and rate of weight gain during pregnancy, by pre-pregnancy BMI

	Total Weight gain		**Rate of weight gain, 2nd and 3rd trimester**	
Pre-pregnancy BMI	**Range in kg**	**Range in lbs**	**Mean (range) in kg / week**	**Mean (range) in lbs / week**
Underweight (<18.5 kg/m^2)	12.5 – 18.0	28.0 – 40.0	0.51 (0.44-0.58)	1.0 (1.0-1.3)
Normal weight (18.5 – 24.9 kg/m^2)	11.5 – 16.0	25.0 – 35.0	0.42 (0.35–0.50)	1.0 (0.8-1.0)
Overweight (25.0 – 29.9 kg/m^2)	7.0 – 11.5	15.0 – 25.0	0.28 (0.23-0.33)	0.6 (0.5-0.7)
Obese (≥30 kg/m^2)	5.0 – 9.0	11.0 – 20.0	0.22 (0.17-0.27)	0.5 (0.4-0.6)

3.4.4 **Maternal body composition**

Maternal body composition was also assessed at each anthropometric visit using SFT measurements. Although many previous studies have estimated maternal body composition using BIA, several possible factors compromise its validity for use in pregnancy, particularly its reliance on the estimation of TBW from the ratio of intracellular water to extracellular water, which changes throughout pregnancy (Widen and Gallagher, 2014). SFT measurements are increasingly being used to assess changes to maternal body composition throughout pregnancy. Typically, changes in FM are estimated using equations that consider SFT, body weight, height, AC and other measurements, but many of these equations have been developed in non-pregnant women and have been shown to overestimate fat changes in pregnancy when

compared with a four-compartment model (Paxton *et al.*, 1998). Skinfold measurements have the added advantage of being generally acceptable to pregnant women, portable for use in the field and inexpensive (Widen and Gallagher, 2014). Kannieappan et al. (2013) developed a standard tool specifically for use with women with obesity that reliably assesses body composition via SFT measured at three sites: biceps, triceps and subscapular, in order to estimate pregnancy-related changes in adipose tissue unrelated to foetal growth. Although other equations, using different equations and skinfold-sites have been developed for use in pregnancy (Paxton *et al.*, 1998; Huston Presley *et al.*, 2000), these equations were developed amongst women of all weights and not specifically for women with obesity. This method has also been employed to assess changes in body composition in a recent mobile intervention to promote healthy GWG in New Zealand (Willcox *et al.*, 2015). As the present study is examining changes in body composition amongst women with obesity, SFT measurements were taken according to the methods described by Kannieappan et al. (2013) and the International Society for the Advancement of Kinanthropometry (ISAK) (Stewart *et al.*, 2011). The researcher collecting these measurements completed the ISAK Level 1 qualification prior to the collection of data and satisfied intra- and inter-observer competencies as part of the assessment process.

The three skinfold sites were located using the correct anatomical landmarks, always on the right-hand side. In order to locate the biceps and triceps sites, the mid-point of the *acromiale* and *radiale* landmarks was located. The *acromiale* landmark is the most lateral part of the acromion border, while the *radiale* landmark is defined as the point

at the proximal and lateral border of the head of the radius. The mid-point of these landmarks was defined as the mid-pint of the straight-line joining the *acromiale* and *radiale* landmarks, which was located using a segmometer (Rosscraft, British Columbia, Canada). An anthropometric tape (Seca 201, Hamburg, Germany) was used to project this mark around to the posterior and anterior surfaces of the arm in a horizontal line. The triceps and biceps skinfold sites were defined as the point on the posterior and anterior surfaces, respectively, at the level of the marked mid-*acromiale-radiale* landmark, which was marked with a horizontal line, with a vertical line placed in the middle of the muscles. Both vertical lines were just visible when standing to the side of the participant.

The *subscapular* skinfold site was located by landmarking the under-most tip of the inferior angle of the scapula, and marking the site 2cm along a line running laterally and obliquely downward from this landmark at a 45º angle. A second line was placed perpendicular to the first in order to indicate the alignment of the finger and thumb when picking up the skinfold.

SFT was measured at each site using Harpeden callipers (British Indicators, Sussex, England) by a single researcher in order to minimise systematic error. At each site the skin and subcutaneous fat were grasped between the thumb and index finger of the left hand – taking care to leave underlying muscle behind. The size of the fold was the minimum necessary to pick up a parallel fold between the two skin surfaces. The calliper was placed perpendicular to the skinfold with the nearer edge of the contact faces of the calliper applied 1cm from the edge of the thumb and fingernail and

allowed to gently squeeze. SFT was recorded to the nearest millimetre two seconds after full release of the calliper, even if the needle was still moving, to ensure standardisation (Martin *et al.*, 1985). The biceps and triceps skinfolds were taken parallel to the long axis of the respective marked sites, while the subscapular skinfold measurement was taken with the fold running obliquely downwards at the marked site.

A full set of all three SFT measurements was completed in order to reduce the effects of skinfold compressibility prior to repeating measurements (Stewart *et al.*, 2011). A second measurement was then taken at each site, and if the difference was greater than 7.5%, a third measurement was taken according to ISAK recommendations. SFT for each site was reported as the mean of two measurements, or the median of three measurements (Stewart *et al.*, 2011).

AC was measured in cm at the mid-*acromiale-radiale* site, previously landmarked for the assessment of triceps and biceps skinfold sites. The participant assumed a relaxed standing position and the anthropometric tape was passed around the arm. Once the cross-taped position was achieved, the mid-*acromiale-radiale* site was situated between the two parts of the tape and measurement recorded to the nearest millimetre.

Mean SFT was reported in mm at each site and as the sum of SFT at the three sites at each study visit. Body fat percentage (BF%), FM and FFM were also calculated and reported using the following equation (Kannieappan *et al.*, 2013):

BF% = 12.7 + (0.457 x triceps SFT) + (0.352 x subscapular SFT) + (0.103 x biceps SFT) – (0.057 x height in cm) + (0.265 x AC in cm)

FM (kg) = body weight (kg) x (%BF/100)

FFM (kg) = body weight (kg) – FM (kg)

Change in FM and FFM were calculated from the difference between values at each study visit to give total, second and third trimester changes in body composition. Rate of change in FM and FFM over the study duration, as well as rates in the second and third trimesters have also been calculated to adjust for gestation for each participant.

3.4.5 **Dietary intake**

The majority of previous studies assessing dietary intake during pregnancy have utilised food frequency questionnaires (FFQs) (Lagiou *et al.*, 2004; Olafsdottir *et al.*, 2006; Stuebe, Oken and Gillman, 2009). Despite FFQs being cited as valid methods of assessing dietary intake (Erkkola *et al.*, 2001; Khani *et al.*, 2004; Mikkelsen, Osler and Olsen, 2006), comparison studies have shown FFQs to be less accurate at estimating average dietary intake when compared with 7 day diet diaries (Brunner *et al.*, 2001; Day *et al.*, 2001) and 3 day diaries (Schroder *et al.*, 2001; Yang *et al.*, 2010).

Although 7 day weighed records are traditionally viewed as the 'gold standard' for dietary assessment (Jain, Howe and Rohan, 1996), weighing all foods and drinks consumed would have placed a large burden on participants. Household measurements are acknowledged as valid methods of dietary assessment, and in many cases prove to be better representative of actual food intake than weighed records especially if participant motivation dips during data collection (Lee and Nieman, 1993).

Dietary intake in the present study was therefore assessed using a 4 day diet diary, as previously validated in the National Diet and Nutrition Survey (NDNS) (Whitton *et al.*, 2011), in order to maximise the validity and reliability of dietary assessment (Appendix 7). The 4 day period following each study visit was chosen in an attempt to maximise compliance with this aspect of data collection, and it was also the same 4 day period that participants were asked to wear an accelerometer for the collection of physical activity data. Previous studies suggest that dietary data collection should include at least one weekend day in order to account for differences in food and energy intakes, which tend to be higher at weekends (An, 2016; Jahns *et al*., 2017). However, in order to maximise compliance, the recording period was not interrupted to accommodate this, nor was it extended beyond 4 days as this would have increased the burden on participants, which may have increased attrition (Cade *et al*., 2017).

Subjects were asked to record, in as much detail as possible, all food and beverages consumed within a 4 day period following each study visit, giving details about their portion sizes using weights, household measurements, packet sizes and photographs. Subjects were also asked to record any dietary supplements, whether prescribed or self-bought. At the end of the 4-day period, the researcher visited the subject to collect the diary and to clarify portion sizes and the types of foods eaten. The researcher also asked the participant to report whether their dietary intake had been affected by complications such as pregnancy sickness or hyperemesis gravidarum. There was a section at the end of each day for women to record whether they

experienced nausea or vomiting and if so, to what extent they believed their appetite or food intake was affected.

Dietary assessment data was analysed using DietPlan 7 (Forestfield Software Ltd 2010, Horsham, West Sussex, UK) to generate nutritional intake data for each participant using data from UK Food Composition Tables (Finglas *et al.*, 2015). Food portion sizes were estimated from the photographs, weights given and household measurements using 'Food Portion Sizes' published by the Food Standards Agency in the UK (Mills and Patel, 2002). When foods were missing from the database, nutrient data was obtained from the manufacturer where possible and added manually to the database. For some foods this was not possible, in which case the researcher chose a food with similar nutrient composition from the database.

In order to identify potential under-reporters, basal metabolic rate (BMR) was estimated from the weight and age of each participant, in each trimester, using the Schofield Equation (Schofield, 1985).

Females:

18-29 years BMR (kcal/day) = 14.8W + 487

30-59 years BMR (kcal/day) = 8.3W + 846

Where W = weight, kg. Kcal = kilocalorie.

In order to predict the likelihood of under-reporting, the ratio of EI to BMR (EI:BMR) was calculated for each participant, in each trimester. EI:BMR ratios of 0.9-1.2 and <0.9 have been shown to be indicative of potential and definite underreporting, respectively (Goldberg *et al.*, 1991) and have been used as a means of estimating the

degree of under-reporting amongst pregnant women in the UK previously (McGowan and McAuliffe, 2012). Women were classified in each trimester as 'normal', 'potential' or 'definite' under-reporters with an EI:BMR ratio of ≥1.2, 0.9-1.2 and <0.9, respectively.

The impact of dietary intake on outcomes was assessed via the impact of individual nutrients, as well as via DPA. In order to examine dietary patterns, average food intake in g/day was calculated for 39 food items, which were pre-defined based on food groups used in other studies examining dietary patterns in pregnant women in the UK (Crozier *et al.*, 2008; Northstone, Emmett and Rogers, 2008; Freitas-Vilela *et al.*, 2017) and are shown in Table 3.3.

Previous studies have been more successful at identifying associations between dietary patterns and pregnancy outcomes using dietary data collected early in pregnancy rather than later pregnancy (Rodríguez-Bernal *et al.*, 2010; Hillesund *et al.*, 2014). Some of the present cohort are also likely to have changed their dietary choices before, during or immediately after completing the food diary at the end of their second trimester in response to a positive GDM diagnosis. Dietary patterns were therefore examined in the first trimester amongst the present cohort as the study was not powered to allow for the exclusion of these women in the second trimester.

Table 3.3 Pre-defined food groups used for DPA

Drinks	**Meat/fish**
Fruit juice	Poultry
Soft drinks	Red meat
Sugar free soft drinks	Processed meat
Tea	White fish
Coffee	Oily fish
	Fried meat, fish or eggs
	Meat pies/pasties
Dairy	**Carbohydrates**
Cheese	White bread/rolls
Dairy milk and cream	Non-white bread/rolls
Eggs	Wholemeal cereals
Full fat spreads	Refined cereals
Reduced fat spreads	Pasta/wheat noodles
Yoghurt	Rice/rice noodles
	Fried potatoes (including chips)
	Roast potatoes
	Other potatoes
	Savoury snacks
Fruit/vegetables	**Sugars**
Fresh fruit	Sugar/honey
Bananas	Cakes/Biscuits
Vegetables	Chocolate
Baked beans	Puddings
Vegetable pies/pastries	**Miscellaneous**
	Pulses
	Nuts/seeds

3.4.6 **Physical activity**

Although DLW is regarded as the gold standard for the assessment of energy expenditure, the large costs associated with its use restrict its use in the present study due to the size of its population (Goldberg *et al.*, 1993). Objective methods for the

measurement of physical activity, such as accelerometry, have been shown to demonstrate a high degree of validity when used to quantify physical activity intensity and duration (Corder, Brage and Ekelund, 2007; Prince *et al.*, 2008).

Accelerometers have been used successfully throughout pregnancy amongst women with obesity (McParlin *et al.*, 2010). Although the preferred site of attachment for an accelerometer is traditionally the waistband (Meijer *et al.*, 1991), Rousham, Clarke & Gross (2006) suggest the ankle, and van Hees et al., (2011) the wrist, as appropriate alternative sites of attachment in order to prevent discomfort in this area for the present population, with the hope of increasing compliance.

Women wore an Actigraph wrist-worn accelerometer (Actigraph wGT3X-BT, Florida, USA) for four days following each study visit, alongside the collection of dietary data. The accelerometer was attached via a disposable wrist strap on the participant's dominant wrist. There has been much debate surrounding the selection of the dominant vs. non-dominant wrist, but no clear consensus has been established (Dieu *et al.*, 2017).

The accelerometer was programmed to collect physical activity data for 4 days following each study visit, and participants were encouraged not to remove their accelerometer during this time. Data was collected using 10 second epochs, but as both the wear time (WT) and scoring algorithms used in analysis were validated using 60 second epochs, the accelerometry data files were reintegrated to 60 second epochs for analysis, as supported by Banda et al. (2016) and Ayabe et al. (2013).

At the data collection period, data on the device was synced and analysed on the corresponding computer software program (Actilife 6.0, Florida, USA).

Data from participants recording ≥3 days of valid accelerometry was included in analyses. A valid day was defined as ≥ 500 minutes of WT as detected by the Troiano technique which defines non-wear as an interval of ≥60 consecutive minutes of zero activity counts (Troiano *et al.*, 2008). WT was reported as number of wear periods, average daily WT and percentage WT.

Freedson's cut points were used to classify time as sedentary (<100 counts per minute (CPM)), light activity (100-1951 CPM), and moderate and vigorous activity (>1951 CPM), (Freedson, Melanson and Sirard, 1998) which have been used in recent studies observing women with obesity (Hayes *et al.*, 2015; Tinius *et al.*, 2016). Freedson bouts were determined as >1951 cpm for at least 10 minutes, while sedentary bouts were determined as <100 cpm for at least 10 minutes. Sedentary breaks were defined as the breaks in sedentary activity.

3.4.7 **The incidence of gestational diabetes mellitus**

Incidence of GDM was recorded for each participant in the study. Plymouth NHS Hospitals Trust routinely test all pregnant women with a BMI ≥ 30 kg/m^2 for GDM via a 2-hour 75g OGTT at 28 weeks gestation. Patients were diagnosed with GDM with a fasting plasma glucose level ≥ 5.3 mmol/litre or a 2-hour plasma glucose level of ≥7.8 mmol/litre (Green, Evans and Montague, 2017). This differs slightly from NICE guidance (National Institute for Health and Care Excellence, 2015), who diagnose GDM if patients have a fasting plasma glucose level of ≥5.6 mmol/litre, while the criteria for

the 2-hour plasma glucose is the same, while the International Association of Diabetes and Pregnancy Study Group (IADPSG) diagnostic criteria is fasting plasma glucose level ≥ 5.1 mmol/litre or 2-hour plasma glucose level ≥8.5 mmol/litre (International Association of Diabetes and Pregnancy Study Groups Consensus Panel, 2010).

NICE guidance states that women diagnosed with GDM should be offered diet and exercise advice in the first instance, but if blood glucose targets are not met within 1-2 weeks metformin should be offered, followed by insulin if targets are still not met. Glibenclamide may also be offered instead of, or in addition to metformin if metformin and/or insulin are not tolerated or declined, respectively (National Institute for Health and Care Excellence, 2015). The method of management was recorded for each diabetic participant.

3.5 Infant outcomes

Infants born prior to week 37 of gestation were defined as pre-term and excluded from the study at birth.

Information concerning the delivery of infants was obtained from hospital notes. This included gestational age at delivery, method of delivery, the incidence of any complications, infant gender, birth weight and head circumference.

Description and classification of infant birth size has varied considerably in the current literature. The term macrosomia refers to newborns exhibiting excessively high birth weights, indicative of foetal overgrowth, regardless of gestational age. Traditionally, macrosomia has been defined as a birth weight equal to, or in excess of 4000g, although recent studies have moved towards a cut-point of 4500g, or even 5000g.

Gaudet et al (2014) suggest macrosomia can be subdivided into Class I (birth weight 4000-4499g), Class II (4500-4999g) and Class III (≥ 5000g) in order to address the variation in cut-points, which is used in the current study.

Birth weight and head circumference centiles and z-scores were calculated from British 1990 reference values (Freeman *et al.*, 1995) using the LMS method (Cole and Green, 1992) (LMS Growth Programme v2.77, Medical Research Council, UK) which adjusted for gestational age and infant gender. Although more recent UK-WHO Growth Charts for 0-4 years have been developed, the UK 1990 reference values remain in use for infants up to 2 weeks of age due to a lack of pre-term and term birth data in the WHO charts (SACN/RCPCH Expert Group, 2007). Infants were classified using conventional cut-offs as SGA (birth weight for gestational age <10th percentile), AGA (birth weight for gestational age ≥10th and <90th percentile) or LGA (birth weight for gestational age ≥90th percentile).

Crown-heel length is not routinely measured in PNHT hospitals, so this was measured by the researcher using a mobile measuring mat (Seca 210, Hamburg, Germany). This measurement was taken as soon after delivery as possible and recorded to the nearest 5 millimetres (Appendix 8). Length centiles and z-scores were calculated from British 1990 reference values (Freeman *et al*, 1995) using LMS software and were adjusted for gestation and age at visit.

There are numerous methods of assessing neonatal body composition, which vary in practicality, cost and accessibility. Upper-arm cross-sectional areas have long been used as simple, non-invasive and inexpensive methods of evaluating the nutritional

status of neonates (Pereira-da-Silva *et al.*, 1999). The upper-arm cross-sectional area may be calculated from the MUAC and triceps skinfold and is thought to better represent the relative contributions of fat and muscle to the total arm area than MUAC or triceps skinfold alone (Excler *et al.*, 1985; Hediger *et al.*, 1998).

For this study a model that calculated an upper arm fat area estimate (UFE) and upper arm muscle area estimate (UME) based on the MUAC and triceps skinfold, that has been previously validated against MRI in children (Rolland-Cachera *et al.*, 1997) was used.

The triceps skinfold and MUAC were recorded using the same measurement techniques previously described for the mother, with mother or father assisting the researcher.

The following calculations were performed and are also depicted in Figure 3.1 (Rolland-Cachera *et al.*, 1997):

Upper arm fat area estimate = UFE, total upper arm area = TUA, upper arm muscle area estimate = UME, MUAC (mm) = C, triceps skinfold (mm) = TS.

$TUA = C^2 / (4\pi)$

UFE = C x (TS/2)

UME = TUA – UFE

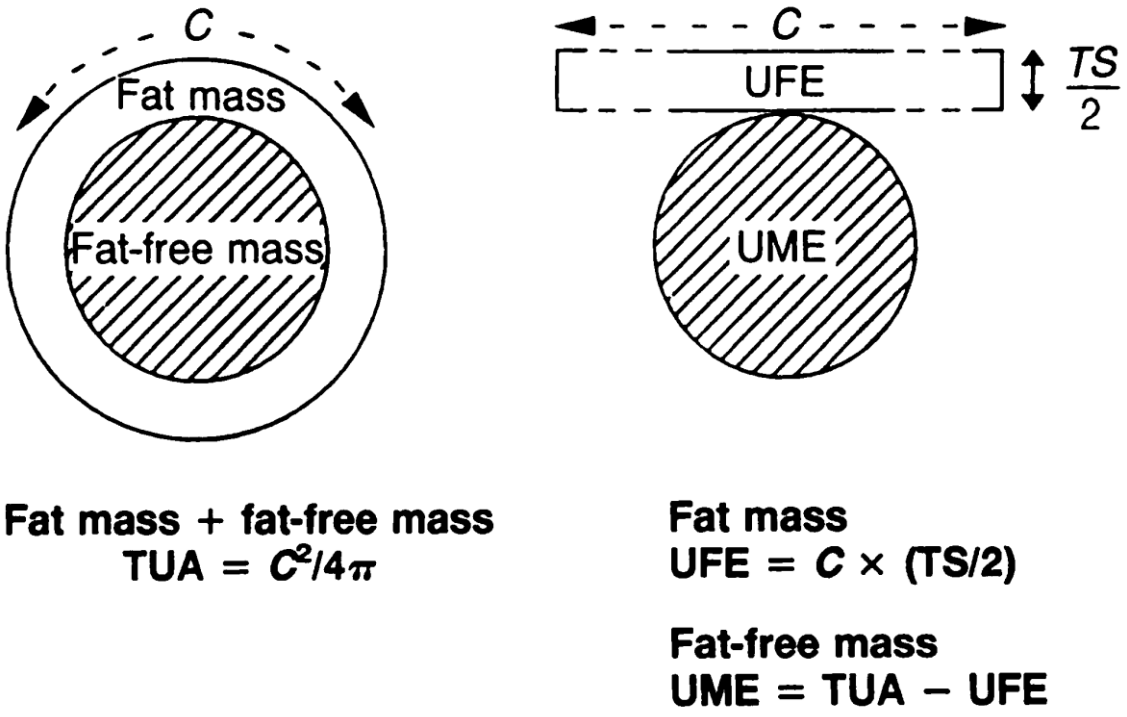


Figure 3.1 Schematic representation of infant arm tissue on which calculations and assumptions are based (Rolland-Cachera et al. 1997).

Carberry et al. (2010) assessed body composition from birth to 4.5 months in infants born to women without obesity, and observed rapid changes in the first 6 weeks of life, with percentage body fat doubling during this period. It was therefore important to measure body composition as soon after birth as possible, as demonstrated by Davenport et al. (2013) who measured skinfolds within 6-18 hours of delivery, and McIntyre et al. (2010) and Sewell et al. (2006), who measured skinfolds within 72 hours of delivery. Anthropometric measurements were taken as close to birth as possible, preferably within 72 hours of delivery. This was not always possible, but measurements taken were adjusted for age where possible.

3.6 Statistical analysis

All data was entered into and analysed using SPSS (Statistics Package for the Social Sciences) for Windows version 21 (IBM, Chicago USA). The level of significance was set to a probability (p) < 0.05 for all statistical tests performed, and unless otherwise stated, data were presented as means ± standard deviation (SD).

Continuous outcome measures were inspected for normality using the Kolmogorov-Smirnov test, when looking at the whole population, and Shapiro-Wilk when looking at sub-samples of the population (Ghasemi and Zahediasl, 2012), plus visual inspection of Q-Q plots and histograms. Data that was normally distributed ($p>0.05$) was analysed using parametric tests. Transformation was attempted on data that was not normally distributed ($p<0.05$) in an attempt to achieve normality. Where normality could not be achieved, non-parametric tests were used.

Pearson's correlation coefficients (r) were run to assess the relationships between maternal anthropometric, maternal diet and infant birth size outcomes.

Independent t-tests and one-way analysis of variance (ANOVA) were performed to explore differences between groups for normally distributed data. Levene's test for equality of variance was performed and homogeneity of variances was assumed if the result was non-significant (for both analyses). If one-way ANOVA was significant, Tukey post-hoc analysis was performed in order to prevent Type I error and to test for all possible combinations of group differences (Westfall *et al.*, 2011). Where the assumption of homogeneity of variances was violated, the Welch t-test or one-way ANOVA was interpreted instead (Lix, Keselman and Keselman, 1996) and post hoc

analysis, if required, was performed using Games-Howell's test (for one-way ANOVA) in order to compare all possible combinations of group differences.

To assess differences between groups for data that were not normally distributed Mann-U Whitney and Kruskall Wallis tests (with pairwise comparisons with adjusted p values) were performed.

Repeated measures one-way ANOVA was performed to determine any differences between dietary intake and physical activity between trimesters for data that was normally distributed. Sphericity was assumed where Mauchly's test of Sphericity was non-significant ($p > 0.05$). Where Mauchly's test of Sphericity was significant, a Greenhouse-Geisser correction factor was applied and posthoc analysis was performed with a Bonferroni adjustment in order to reduce both Type I and Type II error (Maxwell, 1980). Freidman's test was used to assess differences between trimesters for data that was not normally distributed. Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons if required.

Principal component analysis was performed on 39 food items in order to derive dietary patterns. The number of factors, or patterns that best represented the data was chosen based on the eigenvalue-one criterion (Kaiser, 1960), interpretation of the scree plot (Cattell, 1966) and the proportion of variance explained by the components, as well as the interpretability of the factor loadings. A Varimax orthogonal rotation was employed to aid interpretability, and a loading of $\geq \pm 0.4$ was considered to have a strong association with that pattern, which also aided with interpretability. Scores for each pattern were derived from SPSS.

Chapter 4 **Description of the cohort**

Women were recruited for this study between January 2015 and December 2016 from the Antenatal Clinic at Derriford Hospital in Plymouth, and data collection was completed in May 2017. As previously described, data on maternal characteristics was collected at baseline, with maternal anthropometry, diet and physical activity data collected at the end of each of the three trimesters of pregnancy. Following delivery, routine data was collected from maternity notes, and for women who continued with the study, infant anthropometric measurements were performed by the researcher in the week following delivery. Maternal, delivery and neonatal data are described and discussed in this chapter.

4.1 Recruitment and follow up

4.1.1 **Description of recruitment**

A total of 838 eligible women meeting inclusion criteria were identified by the research midwife based on their antenatal booking form. The majority of women were unsuitable or the researcher was unable to attend the clinic, while a further 140 declined the invitation to participate (Table 4.1). A total of 242 women were approached at antenatal clinic in Derriford Hospital, Plymouth, and of these, 102 women (42%) agreed to participate in the study. Reasons for non-participation are also shown in Table 4.1. Upon recruitment, a provisional first appointment to take consent and first measurements was arranged. Of these women, 76 (75%) kept this appointment and were enrolled in the study, which was just 31% of women approached. Sadly, one woman was advised to end her pregnancy at 20 weeks after

receiving news at a foetal anomaly scan. This participant's data has therefore not been included in analysis. Table 4.2 shows reason for dropout between recruitment and consent.

Table 4.1 Description of women identified as eligible to participate in the study

	Eligible women at 12 week scan n=838 (%)
Suitable and willing to participate	102 (12)
Refused	140 (17)
Missed by researcher	516 (62)
Ineligible	79 (9)
Ethnicity	6
BMI <30 or ≥40 kg/m^2	12
Medical reason	5
Maternal age >40	1
Home address outside Plymouth	1
Advanced gestation	1
Participation in other research projects	19
Miscarriage	24
Twin pregnancy	4
High risk of trisomy	1
Termination of pregnancy	3
Previous participation in study	2
Reason for refusal	**n = 140 (%)**
No reason given	124 (89)
Not enough time	13 (9)
Uncomfortable with measurements	3 (2)

Table 4.2 Description of women recruited into the study

	Women recruited (%) n = 102
Consented and enrolled	76 (75)
Dropout	26 (26)
Reason for dropout	n= 26 (%)
No answer at door/couldn't contact	7 (27)
Changed mind – too busy	5 (19)
Changed mind – no reason given	11 (42)
Medical reason	2 (8)
Miscarriage	1 (4)

4.1.2 **Description of the participants**

A description of the 75 women who consented to participate is show in Table 4.3. Participants' ages ranged from 19 years to 40 years, with mean age of 29.8 ± 4.8 years. Of the 75 women, 62 (83%) were classified as having Class I obesity, with the remainder classified as Class II. Obstetric history varied considerably, with 28 (37%) nulliparous women, and parity ranging from 1 to 5 for the remaining women.

Table 4.3 Description of the study participants at recruitment n= 75 (%)

	Mean	**Range**	**SD {CI}**
Age (years)	29.8	19.0 - 40.0	4.8
BMI at booking (kg/m^2)[b]	32.7	30.0 - 37.6	(3.4)
Weight at booking (kg)[a]	88.4	73.0 – 118.4	{86.5-90.4}
Height (m)	1.64	1.51-1.77	0.06
Parity[b]	1.0	0.0 – 5.0	1.0
Index of Multiple Deprivation Rank[b]	10444	356 – 29651	(18203)
Index of Multiple Deprivation Decile[b]	4.0	1.0 -10.0	(5.0)
	n (%)		**n (%)**
BMI class:		**Parity:**	
Obese Class I (≥30 BMI kg/m^2 <35)	62 (83)	Nulliparous	28 (37)
Obese Class II (≥35 BMI kg/m^2 <40)	13 (17)	≥ 1	47 (63)
Pre pregnancy smoker:		**Pregnancy smoker:**	
Yes	15 (20)	Yes	8 (11)
No	60 (80)	No	67 (89)

[a]Mean calculated by back-transformation {confidence intervals}.
[b]Expressed as median (interquartile range)

The median Index of Multiple Deprivation rank was 1044, while the median decile was 4 and ranged from 1 to 10 amongst participants. A total of 33 (44%) women took a supplement containing folic acid prior to conception, and 71 (95%) were taking a

supplement by the end of their first trimester. A total of 15 (20%) women were smokers before becoming pregnant and 8 women (11%) planned to continue smoking during their pregnancy.

Women were asked to self-report whether they suffered from pregnancy sickness, and if so, whether their appetite was affected (Table 4.4). Just 2 women were diagnosed with hyperemesis gravidarum during their pregnancy.

Table 4.4 Reported pregnancy sickness amongst participants

	Women (%) **n = 75**
Pregnancy sickness reported	60 (80)
Appetite affected by pregnancy sickness	58 (77)
Hyperemesis gravidarum diagnosed	2 (3)

All women who participated lived in Plymouth. Figure 4.1 shows the distribution of home postcodes at enrolment for the 75 participants.

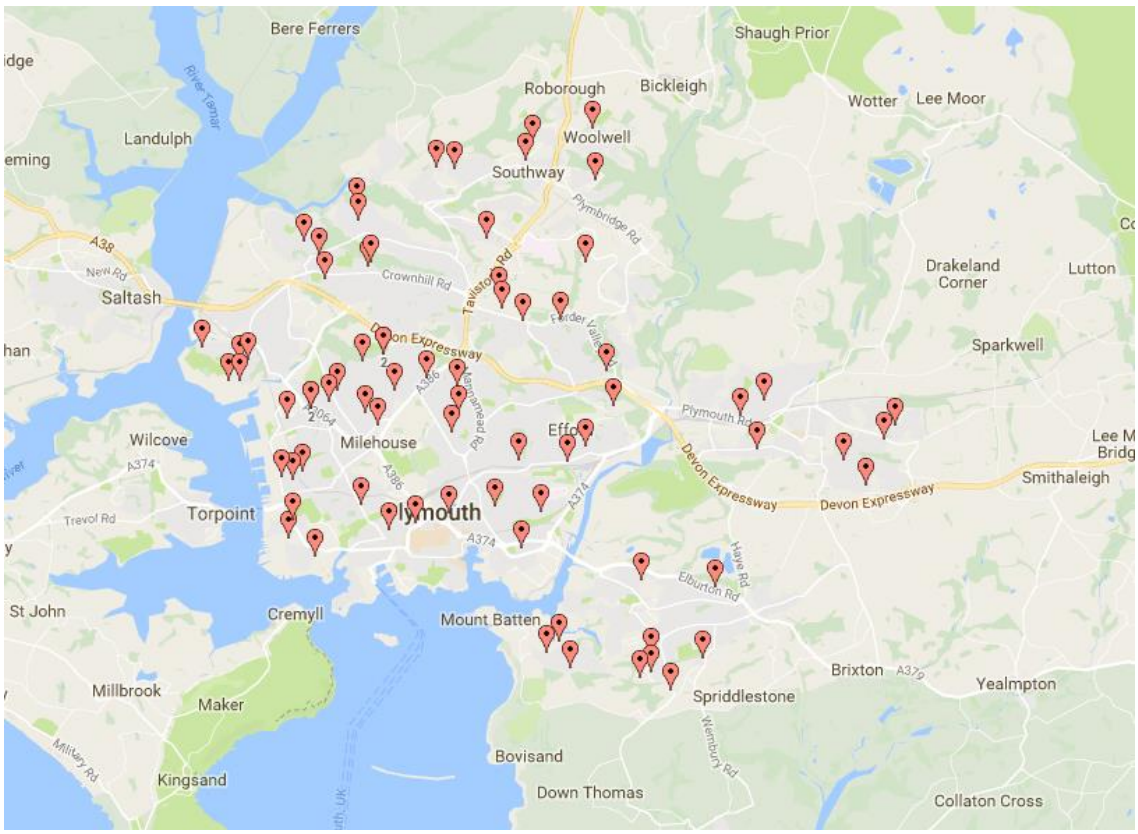


Figure 4.1 Distribution of home postcodes of women enrolled in the study. Created using Google Maps.

4.1.3 **Follow up of participants during pregnancy**

After consenting at study visit 1, participants were followed up on two further occasions at study visits 2 and 3, at the end of the second and third trimesters respectively. Table 4.5 shows the length of gestation for participants who kept these appointments.

Table 4.5 Length of gestation at each study visit

	Median	Range	IQR
Study visit 1 (n=75)			
Gestation (days)	90.0	82-108	5.0
Gestation (weeks^{+days})	12^{+6}	11^{+5}-15^{+3}	-
Study visit 2 (n=65)			
Gestation (days)	200	190-209	6.0
Gestation (weeks^{+days})	28^{+4}	27^{+1}-29^{+6}	-
Study visit 3 (n=57)			
Gestation (days)	255	250-266	5.0
Gestation (weeks^{+days})	36^{+3}	35^{+5}-38^{+0}	-

There was considerable variation in compliance with the three main study outcome measures: anthropometrics, diet and accelerometry at each study visit. Table 4.6 shows the compliance of participants with each outcome measure at each stage of the study, as well as those lost to follow up. At study visit 1, data was collected for all 75 participants, although full datasets comprising of anthropometric, diet and accelerometry data was only collected for 58 participants (77%), while partial data was collected for the remaining participants. Between study visits 1 and 2, 10 participants (13%) were lost to follow up, while full data was collected for 49 participants (65%) and partial data collected for the remaining 16 participants. By study visit 3 a total of 16 participants (21%) has been lost to follow up, with full data collected for 46 participants (61%) and partial data collected for a further 13 participants. Reasons for non-compliance and loss to follow up are also shown in Table 4.6.

Table 4.6 Compliance with study procedures throughout pregnancy (n=75)

	Compliant women (%)		
	Study visit 1 (n=75)	**Study visit 2 (n=65)**	**Study visit 3 (n=59)**
Compliance			
Anthropometrics + diet + accelerometry	58 (77)	49 (65)	46 (61)
Anthropometrics + diet only	9 (12)	9 (12)	6 (8)
Anthropometrics + accelerometry only	5 (7)	3 (4)	1 (1)
Anthropometrics only	3 (4)	4 (5)	6 (8)
Non-compliance			
Diet + accelerometry	**3**	**4**	**6**
Unwilling/unable	3	4	6
Diet only	**5**	**3**	**1**
Incomplete diary	2	1	-
Lost diary	3	2	1
Accelerometry only	**9**	**9**	**6**
Accelerometer failure	4	2	-
Insufficient wear time	3	6	6
Occupation	1	1	-
Unwilling/unable	1	-	-
Lost to follow up	**0 (0)**	**10 (13)**	**16 (21)**
Unable to contact	-	9	2
Withdrew – time commitment	-	1	-
Delivered baby early	-	-	4
Lost to follow-up at previous visit	-	-	10

4.2 Maternal anthropometrics

Weight and body composition measurements for women in trimesters one, two and three are shown in Table 4.7. Maternal weight increased as pregnancy became more advanced, increasing from 89.7 ± 8.7 kg at the end of trimester 1, to 95.1 ± 9.2 kg and 97.0 ± 9.9 kg at the end of trimesters 2 and 3, respectively. GWG in each of the

trimesters and across pregnancy also varied considerably between participants. Mean total GWG was 7.5 ± 6.2 kg with some women experiencing gestational weight loss (GWL) of up to 6.6 kg and others GWG up to 22.2 kg.

Changes in maternal body composition also varied widely. Mean percentage body fat did not change much for the population from trimester 1 (40.3 ± 4.5%) to trimester 2 (40.9 ± 5.5%) and trimester 3 (39.5 ± 5.8%), however on an individual level, total change in %BF across pregnancy ranged from a loss of 10.3% to an increase of 13.2% with a mean change of -0.9 ± 5.3%.

Table 4.7 Maternal anthropometric measurements

	Trimester 1 (n=75)	**Trimester 2 (n=65)**	**Trimester 3 (n=57)**
GWG			
Weight (kg)	89.7 ± 8.7 (73.0-117.0)	95.1 ± 9.2 (77.6 – 124.0)	97.0 ± 9.9 (77.6 – 125.4)
GWG from previous trimester (kg)	0.9 ± 3.2 (-9.0-12.4)	5.2 ± 3.7 (-4.8 – 13.0)	2.3 ± 3.2 (-4.0 – 9.2)
Total GWG from visit 1 (kg)	-	-	7.5 ± 6.2 (-6.6 – 22.2)
Rate of GWG from previous trimester (kg/week)	-	0.33 ± 0.23 (-0.31-0.87)	0.29 ± 0.40 (-0.50 – 1.26)
Total rate of GWG from visit 1 (kg/week)	-	-	0.32 ± 0.26 (-0.28 – 0.91)
AC (cm)	35.2± 2.7 (30.0 – 43.5)	34.8 ± 2.8 (28.2 – 41.8)	34.3 ± 3.0 (27.5 – 40.5)
SFT			
Triceps SFT (mm)	29.56 ± 5.2 (14.4-43.1)	30.4 ± 5.9 (17.4 – 44.4)	28.5 ± 5.7 (17.3 – 41.7)
Biceps SFT (mm)	18.9 {17.6-20.3}[a] (9.3-46.7)	19.1 ± 6.0 (6.6 – 34.5)	18.0 ± 6.4 (6.0 – 33.0)
Subscapular SFT (mm)	34.2 ± 7.5 (21.4-54.6)	35.4 ± 9.0 (19.3 – 57.8)	34.5 ± 8.5 (26.1 – 55.2)
Σ 3 sites (mm)	83.7 ± 13.6 (57.9-134.7)	85.0 ± 15.0 (54.1 – 121.4)	81.0 ± 17.1 (43.2 – 126.4)

Body fat (%)			
Body fat (%)	40.3 ± 4.5 (31.2-53.9)	40.9 ± 5.5 (29.1 – 56.6)	39.5 ± 5.8 (26.1 – 55.2)
Change in BF from previous trimester (%)	-	0.4 ± 3.7 (-6.5-11.2)	-1.26 ± 3.4 (-7.6- 9.2)
Total change in BF from visit 1 (%)	-	-	-0.9 ± 5.3 (-10.3 - 13.2)
FM			
FM (kg)	35.8 {34.4-37.2}[a] (23.6 – 63.1}	39.1 ± 8.1 (25.2 ± 66.8)	38.7 ± 8.4 (22.1 – 61.7)
Change in FM from previous trimester (kg)	-	2.6 ± 4.6 (-5.5 – 15.2)	-0.1 ± 4.1 (-7.9 – 9.7)
Rate of change in FM from previous trimester (kg/week)	-	0.16 ± 0.28 (-0.32-0.93)	0.00 ± 0.53 (-0.98– 1.44)
Total change in FM from visit 1 (kg)	-	-	2.4 ± 7.0 (-9.2 – 21.3)
Total rate of change in FM from visit 1 (kg/week)	-	-	0.10 ± 0.30 (-0.42 – 0.88)
FFM			
FFM (kg)	53.4 ± 5.1 (42.9 – 68.0)	56.0 ± 5.1 (46.0 – 67.9)	58.4 ± 5.7 (42.0 – 73.7)
Change in FFM from previous trimester (kg)	-	2.6 ± 3.1 (-5.6 – 8.4)	2.4 ± 2.6 (-7.3 – 8.0)
Rate of change in FFM from previous trimester (kg/week)	-	0.17 ± 0.20 (-0.37-0.56)	0.29 ± 0.33 (-1.08 – 1.02)
Change in FFM from visit 1 (kg)	-	-	5.1 ± 3.7 (-6.2 – 15.3)
Rate of change in FFM from visit 1 (kg/week)	-	-	0.21 ± 0.16 (-0.26 – 0.64)

Mean ± SD (range)
[a]Mean calculated by back-transformation {CI}

4.2.1 **Adherence to Institute of Medicine gestational weight gain guidelines**

The IOM (Rasmussen and Yaktine, 2009) recommend that women gain 0-2kg in the first trimester of pregnancy, regardless of pre-pregnancy BMI. Second and third trimester recommendations are based on pre-pregnancy BMI. IOM recommendations state that women with a pre-pregnancy BMI ≥30 kg/m^2 should gain 5-9kg in total over their pregnancy, which taking first trimester recommendations into account, equates

to a rate of weight gain of 0.17-0.24 kg/week in the second and third trimesters. Table 4.7 shows that mean rate of GWG in trimester 2, 3, and in total over pregnancy was 0.33 ± 0.23, 0.29 ± 0.40 and 0.32 ± 0.26 kg/week, respectively.

Table 4.8 Participants in each IOM category for GWG

	Insufficient (%)	Adequate (%)	Excessive (%)
Trimester 1 (n=75)	36 (48)	13 (17)	26 (35)
Trimester 2 (n=65)	17 (26)	10 (15)	38 (59)
Trimester 3 (n=57)	23 (40)	3 (5)	31 (54)
Mean rate across trimesters 2 and 3 (n=57)	16 (28)	8 (14)	33 (58)

Table 4.8 shows the proportion of women gaining below, within and above these recommendations for each of the three trimesters. For trimesters two and three rate of GWG was adjusted for gestation. The proportion of participants gaining in excess of IOM guidelines in trimesters one, two and three, was 35%, 59% and 54%, respectively.

4.2.2 **Gestational weight loss**

Of the women who gained 'insufficient' weight according to IOM guidelines, some women lost weight during their pregnancy, while other women gained weight which was below guidelines (Table 4.9).

In trimester 1, 36 women gained insufficient weight according to IOM guidelines (<0.5kg). Of these women, 28 experienced GWL which ranged from 8.95 kg to 0.2kg loss, while 8 women gained ≥0.0 and <0.5kg. In trimesters 2 and 3, 3 and 11 women experienced GWL, respectively, which was based on rate of GWL/GWG. Over total pregnancy, 8 women lost weight between study visit 1 and 3, which ranged from GWL of -6.6kg to 0.2kg.

Table 4.9 Women gaining below IOM GWG guidelines

	GWL	GWG < IOM guidelines
Trimester 1 (n=36)		
Women (n)	28	8
GWG/GWL (kg)	-2.2 ± 1.8 (-8.95 - -0.2)	0.1 ± 0.1 (0.0 – 0.3)
Trimester 2 (n=17)		
Women (n)	3	14
GWG/GWL (kg)	-2.6 ± 1.9 (-4.8 – -1.2)	1.2 ± 0.9 (0.0 – 2.6)
GWG/GWL (kg/week)	-0.17 ± 0.12 (-0.31 - -0.09)	0.08 ± 0.06 (0.00 – 0.158)
Trimester 3 (n=23)		
Women (n)	11	12
GWG/GWL (kg)	-2.3 ± 1.2 (-4.0 - -0.2)	0.6 ± 0.5 (0.0 – 1.4)
GWG/GWL (kg/week)	-0.30 ± 0.15 (-0.50 - -0.03)	0.08 ± 0.06 (0.00 – 0.16)
Total (n=16)		
Women (n)	8	8
GWG/GWL (kg)	-3.2 ± 1.9 (-6.6 - -0.2)	2.6 ± 0.9 (1.4 – 3.8)
GWG/GWL (kg/week)	-0.13 ± 0.08 (-0.28 - -0.01)	0.11 ± 0.04 (0.06 – 0.16)
Mean ± SD (range)		

4.2.2.1 Composition of gestational weight gain by Institute of Medicine category

Table 4.10 shows the difference in GWG, FM and FFM between visit 1 and 2, visits 2 and 3 and total over pregnancy (between visits 1 and 3). In trimester 2, Welch's one-way ANOVA revealed statistically significant differences between IOM categories for trimester 2 rate of GWG and rate of FM accrual ($p<0.01$), but not for rate of FFM accrual. Unsurprisingly, Games Howell posthoc analysis revealed statistically significant differences in rate of GWG between all three IOM categories. For FM, Tukey posthoc analysis revealed that those classified as gaining in excess of IOM guidelines had significantly higher gains in FM (0.304 ± 0.259 kg/week) than those gaining within (0.042 ± 0.175 kg/week, $p<0.01$) and below the guidelines (-0.090 ± 0.154 kg/week,

$p<0.01$), with no differences between those gaining within and below the guidelines ($p>0.05$). Figure 4.2 shows these changes graphically.

As in trimester 2, one-way ANOVA revealed statistically significant differences between IOM categories for trimester 3 rate of GWG and rate of FM accrual ($p<0.01$), but not for rate of FFM accrual. Tukey posthoc analysis revealed statistically significant differences in rate of GWG between those gaining above and within and above and below IOM guidelines. For FM, Tukey posthoc analysis revealed a statistically significant difference between those gaining above (0.314 ± 0.445 kg/week) and below the guidelines (-0.427 ± 0.326 kg/week, $p<0.01$) but no other differences between rate of FM accrual and any other IOM category. Figure 4.3 shows these changes graphically.

As per trimester 2 and 3, one-way ANOVA revealed statistically significant differences between IOM categories for total rate of GWG and rate of FM accrual ($p<0.01$) but not for FFM accrual. Games Howell posthoc analysis showed statistically significant differences between rate of total GWG and rate of FM accrual between all IOM categories with rate of GWG and FM accrual increasing from those gaining below to within and above the IOM guidelines ($p<0.01$). Figure 4.4 shows these changes graphically.

Table 4.10 GWG, FM and FFM by IOM category (n=65)

	Insufficient)	Adequate	Excessive	p
Trimester 2 (n=65)				
GWG, kg/week	0.033 ± 0.116	0.226 ± 0.026	0.490 ± 0.137	<0.0005
FM gain, kg/week	-0.090 ± 0.154	0.042 ± 0.175	0.304 ± 0.259	<0.0005
FFM gain, Kg/week	0.122 ± 0.170	0.188 ± 0.166	0.187 ± 0.217	0.519
Trimester 3 (n=57)				
GWG, kg/week	-0.101 ± 0.221	0.218 ± 0.034	0.593 ± 0.232	<0.0005
FM gain, kg/week	-0.427 ± 0.326	0.087 ± 0.273	0.314 ± 0.445	<0.0005
FFM gain, Kg/week	0.329 ± 0.230	0.131 ± 0.274	0.279 ± 0.395	0.602
Total (n=57)				
GWG, kg/week	-0.011 ± 0.139	0.216 ± 0.029	0.498 ± 0.143	<0.0005
FM gain, kg/week	-0.210 ± 0.141	-0.017 ± 0.077	0.282 ± 0.239	<0.0005
FFM gain, kg/week	0.199 ± 0.114	0.233 ± 0.091	0.217 ± 0.185	0.873
Mean ± SD, one way ANOVA				

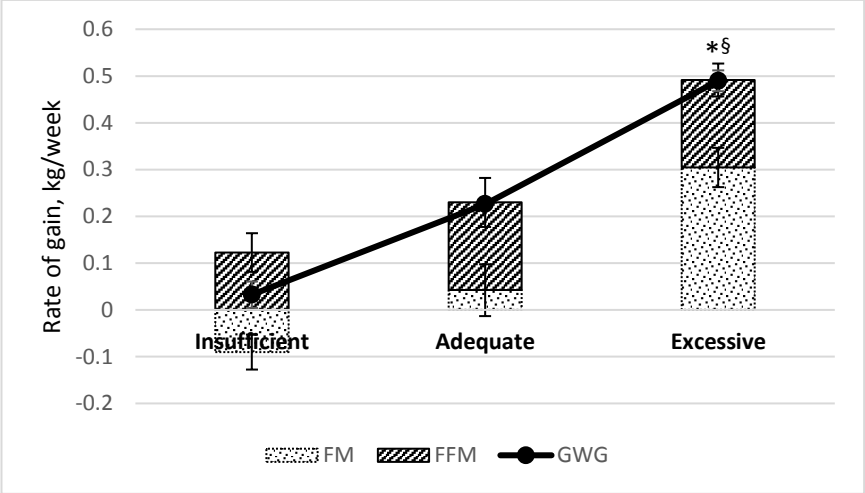


*Figure 4.2 Trimester 2 GWG, FM and FFM by IOM category. Change in FM: *p<0.01 compared to insufficient, §p<0.01 compared to adequate.*

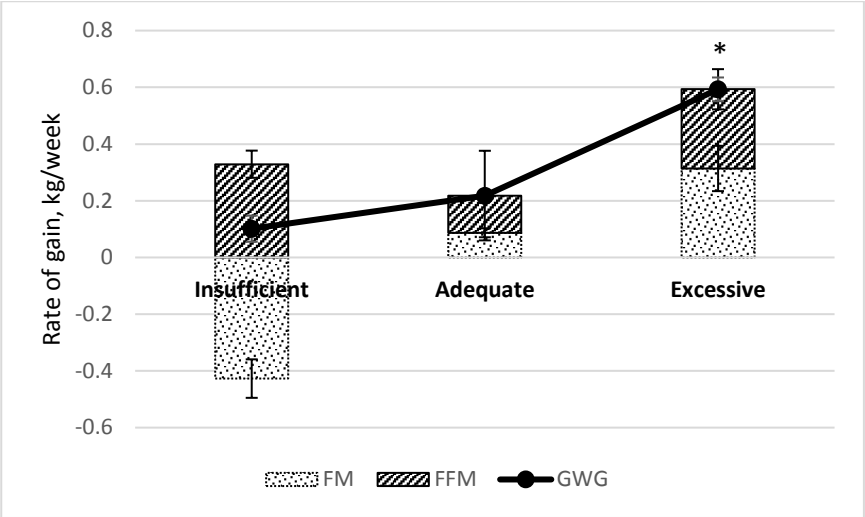


*Figure 4.3 Trimester 3 GWG, FM and FFM by IOM category. Change in FM: *p<0.01 compared to insufficient*

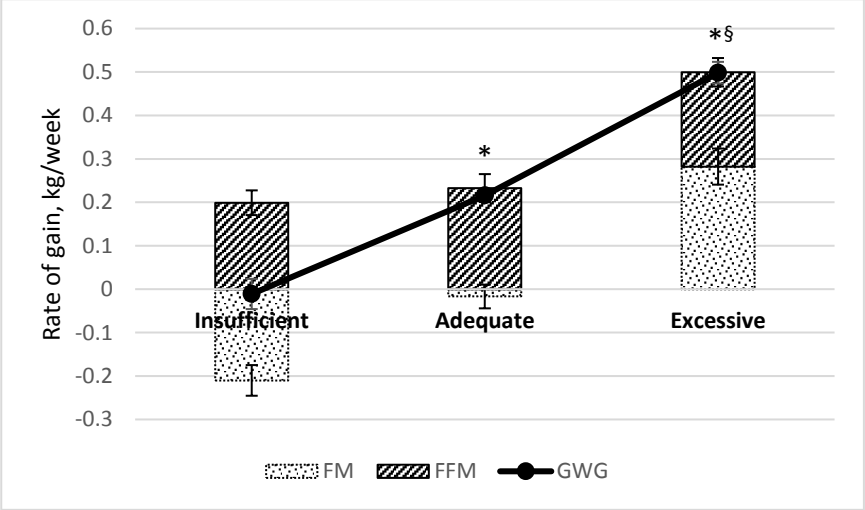


*Figure 4.4 Total GWG, FM and FFM by IOM category. Change in FM: *p<0.01 compared to insufficient, §p<0.01 compared to adequate*

4.3 Prevalence of GDM

As all participants were classified as having a BMI ≥ 30 kg/m^2, they all received an OGTT at the end of their second trimester. Incidence of GDM, as defined by PNHT guidance (see Chapter 3), for the study population is shown in Table 4.11 alongside the management strategies employed by diagnosed women to manage their GDM. In

total, 19 women (25%) were diagnosed with GDM, and of these women, management data was available for 14 women. Four women successfully controlled their GDM by making changes to their diet and lifestyle, while 6 were prescribed Metformin, and a further 4 women required the addition of insulin to manage their diagnosis.

Table 4.12 shows maternal booking characteristics by GDM diagnosis. No statistically significant differences were observed between groups.

Table 4.11 OGTT results (n=75)

OGTT blood test results	**n=73**
Fasting glucose (mmol/l)[a]	4.50 (0.55)
2 hour glucose (mmol/l)[a]	5.90 (1.40)
Diagnosis	**n=75 (%)**
Positive OGTT	19 (25)
Negative OGTT	53 (71)
Missing results	3 (4)
Management	**n=19 (%)**
Lifestyle change	4 (21)
Metformin	6 (32)
Metformin and Insulin	4 (21)
Missing data	5 (26)
[a]Median (IQR)	

Table 4.12 Maternal booking characteristics by GDM diagnosis

	+ve GDM diagnosis (n=19)	**-ve GDM diagnosis (n=53)**	**p**
Age (years)	30.84 ±5.51	29.42 ± 4.73	0.284
BMI at booking (kg/m^2)[a]	33.46 (3.65)	32.45 (2.83)	0.623
Weight at booking (kg)	88.2 ± 8.2	89.1 ± 8.9	0.707
Height (m)	163.68 ± 6.02	164.44 ± 5.69	0.626
Parity (n)[a]	0.00 (1.00)	1.00 (1.50)	0.144
Index of Multiple Deprivation Rank[a]	12757	10126	0.135
Index of Multiple Deprivation Decile[a]	4.0	4.0	0.128
Mean ± SD, independent t test (2 tailed)			
[a]Median (IQR), Mann-Whitney U Test			

4.4 Maternal diet

Table 4.13 Macronutrient intake by trimester for all women

	Trimester 1 (n=66)	Trimester 2 (n=58)	Trimester 3 (n=52)
Energy			
Energy (kcal)	1766 ± 443	1829 ± 418	1910 ± 452
Carbohydrate (CHO)			
Total CHO (g)	235.3 ± 64.3	227.9 {212.8-244.0}[a]	240.6 ± 64.2
Energy from CHO (%)	53.4 ± 6.8	51.6 ± 6.7	50.5 ± 7.0
Starch (g)	123.2 ± 33.6	125.3 ± 34.9	127.2 ± 39.0
Total sugars (g)	89.9 {80.6 -100.3}[a]	86.4 {76.9 – 97.1}[a]	96.8 ± 45.3
Energy from sugars (%)	21.1 {19.5 – 22.7}[a]	20.7 ± 7.2	20.1 ± 7.2
Fibre (g)	16.9 ± 5.0	17.1 ± 4.3	16.9 ± 5.0
Fat			
Total fat (g)	67.9 ± 21.1	70.8 ± 21.0	76.5 ± 25.6
Energy from fat (%)	34.5 ± 4.8	34.5 ± 5.5	35.7 ± 6.5
Saturated fat (g)	24.1 ± 8.9	26.0 ± 8.8	28.7 {25.5 – 32.0}[a]
Energy from saturated fat (%)	12.1 ± 2.6	12.7 ± 2.8	13.6 {12.6 – 14.6}[a]
Protein			
Protein (g)	67.7 ± 20.7	75.8 ± 19.2	78.6 ± 18.8
Energy from protein (%)	15.1 {14.4 – 15.9}[a]	16.5 {15.7 – 17.3}[a]	16.5 {15.6 - 17.3}[a]

Mean ± SD (range)

[a]Mean calculated by back-transformation {CI}

As previously reported in Table 4.6, the number of women completing at least three days of dietary records decreased across the trimesters. Table 4.13 shows mean energy and macronutrient intakes for women who completed diet diaries in trimester 1 (n=66), trimester 2 (n=58) and trimester 3 (n=52).

Table 4.14 shows the proportion of women expected to be 'potential' or 'definite' under-reporters of dietary intakes as defined by their EI to BMR ratio, as calculated using the Schofield (1985) equation and using Goldberg (1991) cut-offs. Approximately

50% of women can be classified as 'potential under-reporters' in each of the three trimesters, while the proportion classified as 'definite under-reporters' was 25.8, 27.6 and 21.2% of women in trimesters 1, 2 and 3, respectively. Many women experienced GWL or pregnancy sickness at one or more time-points during their pregnancy which may explain decreased EI and therefore, no women have been excluded from the main analysis based on under-reporting. Analysis of data excluding 'definite under-reporters' is available in Appendix 9.

Table 4.14 Assessment of energy underreporting according to Goldberg (1991) cut-offs for all women.

	Trimester 1 (n=66) n (%)	**Trimester 2 (n=58) n (%)**	**Trimester 3 (n=52) n (%)**
Normal reporters (EI:BMR ≥1.2)	16 (24)	13 (22)	15 (29)
Potential under-reporters (EI:BMR ≥0.9 and <1.2)	33 (50)	29 (50)	26 (50)
Definite under-reporters (EI:BMR <0.9)	17 (26)	16 (28)	11 (21)

To look at differences in nutrient intakes over the course of pregnancy a repeated measures one-way ANOVA was performed on data from women who completed diaries in all three trimesters who did not develop GDM (n=34; Table 4.15).

Table 4.15 Macronutrient intake across trimesters for women without GDM (n=34)

	Trimester 1	Trimester 2	Trimester 3	p
Energy				
Energy (kcal)	1870 ± 410	1840 ± 358	1975 ± 413	0.152
CHO				
Total CHO (g)	249.0 ± 56.7	239.7 ± 54.0	252.1 ± 51.8	0.549
Energy from CHO (%)	53.7 ± 6.7	52.1 ± 4.8	51.3 ± 4.9	0.132
Starch (g)	131.3 ± 31.3	127.0 ± 29.8	127.5 ± 33.7	0.772
Total sugars (g)	99.6 ± 37.6	95.6 ± 33.1	104.8 ± 36.5	0.559
Energy from sugars (%)[a]	20.5 {18.5-22.7}	20.1 {18.4-21.9}	20.3 {18.5-22.7}	0.939
Fibre (g)	16.8 ± 4.8	16.4 ± 4.1	17.2 ± 5.5	0.625
Fat				
Total fat (g)	71.9 ± 20.3	71.2 ± 16.9	78.7 ± 22.5	0.066
Energy from fat (%)	34.3 ± 4.5	34.8 ± 4.6	35.5 ± 5.0	0.407
Saturated fat (g)	26.2 ± 8.6	26.5 ± 7.1	30.6 ± 10.6	0.021*
Energy from saturated fat (%)	12.4 ± 2.2	13.0 ± 2.4	13.7 ± 2.8	0.067
Protein				
Protein (g)	71.7 ± 22.4	73.3 ± 17.4	79.2 ± 17.1	0.047*
Energy from protein (%)	15.3 ± 2.9	16.0 ± 2.8	16.2 ± 2.4	0.297

Mean ± SD (range)
[a]Mean calculated by back-transformation {CI}

Intake of saturated fat significantly changed across trimesters from 26.2 ± 8.6 g and 26.5 ± 7.1g in trimesters 1 and 2, respectively, to 30.6 ± 10.6g in trimester 3 ($F(2,66) = 4.119$, $p = 0.021$). However, although approaching significance, posthoc analysis with a Bonferroni adjustment did not reveal any statistically significant differences between trimester 1 and 3 ($p = 0.071$) nor between trimester 2 and 3 ($p=0.077$). One-way repeated measure ANOVA also suggested a significant difference between intakes of protein across trimesters, with intakes increasing from 71.7 ± 22.4g to 73.3 ± 17.4g to 79.2 ± 17.1g in trimester 1, 2 and 3, respectively ($F(2, 66) = 3.211$, $p =0.047$). However, once again posthoc analysis with a Bonferroni adjustment did not reveal any statistically significant differences between trimesters. Total energy and fat intakes appeared to be higher in the third trimester compared with the first, but these trends did not reach significance ($p= 0.152$ and $p=0.066$, respectively.)

4.4.1 **Dietary patterns**

Principal components analysis (PCA) revealed fifteen dietary components that had eigenvalues greater than one and which explained from 11.9% to 2.8% of the total variance. Visual inspection of the scree plot indicated that six components should be retained (Cattell, 1966). However, a five-component solution met the interpretability criterion and components 1-5 each met >5% of the total variance, with the 5-component solution explaining 35.1% of the total variance. The five-component solution also exhibited 'simple structure' on the rotated solution, and thus ensured there was no overlap between factors. As such, five components were retained. Of the

39 food groups included in the analysis, 29 had a loading of greater than 0.4 for at least one of the five dietary patterns. Pattern loadings of the rotated solution are presented in Table 4.16.

Pattern 1 was characterised by high intakes of dairy foods (milk, cheese and yoghurt), wholemeal cereals, white fish or seafood and roast potatoes, and low intakes of chips and processed meat. Pattern 2 was characterised by high intakes of poultry, vegetables, nuts and seeds, rice, red meat and sugar free soft drinks. Pattern 3 was characterised by high intakes of white bread, butter, added sugar, baked potatoes, cakes and biscuits, and by low intakes of wholemeal bread. Pattern 4 was characterised by high intakes of eggs and fresh fruit, and low intake soft fruit juice, pulses and refined cereals, while Pattern 5 was characterised by high intakes of baked beans, pasta/noodles and chocolate and low intakes of coffee.

Table 4.16 Trimester 1 factor loading for dietary patterns

Food	Pattern 1	Pattern 2	Pattern 3	Pattern 4	Pattern 5
Percentage variance explained %	**8.6**	**7.7**	**6.9**	**6.0**	**6.0**
Fruit juice	0.124	-0.23	-0.113	**-0.544***	0.255
Soft drinks	-0.251	-0.032	-0.266	-0.316	-0.102
Sugar free soft drinks	-0.360	**0.503***	0.276	0.068	-0.002
Tea	0.320	-0.015	0.245	0.354	-0.162
Coffee	0.006	-0.286	0.143	0.363	**-0.464***
Poultry	-0.157	**0.657***	-0.181	0.147	-0.209
Red meat	-0.050	**0.420***	-0.024	-0.208	-0.079
Processed meat	**-0.479***	-0.025	0.122	-0.022	0.390
White fish and seafood	**0.424***	-0.042	-0.115	-0.350	-0.002
Oily fish	0.330	-0.048	0.068	0.099	0.056
Fried meat, fish or eggs	-0.203	-0.129	-0.015	0.028	0.104
Meat pies or pasties	-0.016	0.117	0.217	-0.197	-0.171
Cheese	**0.429***	0.000	0.190	-0.142	0.089
Dairy milk or cream	**0.674***	-0.268	0.080	-0.083	0.012
Eggs	0.064	0.310	-0.120	**0.586***	0.207
Full fat spreads	-0.151	-0.260	**0.671***	0.210	-0.195
Reduced fat spreads	0.268	0.164	-0.106	0.080	0.393
Yoghurts	**0.441***	0.036	-0.250	0.277	0.181
White bread	0.054	0.097	**0.713***	-0.041	0.152
Non-white bread	0.131	0.177	**-0.406***	0.284	0.098
Wholemeal cereals	**0.555***	0.005	-0.024	0.001	0.203
Refined cereals	0.028	0.037	0.100	**-0.442***	0.085
Pasta/egg noodles	-0.187	-0.115	-0.130	-0.062	**0.571***
Rice/rice noodles	0.070	**0.491***	-0.095	0.018	0.028
Fried potatoes	**-0.623***	-0.071	-0.054	-0.098	-0.151
Roast potatoes	**0.510***	0.232	-0.212	-0.008	-0.391
Other potatoes	0.018	0.049	**0.517***	-0.127	-0.046
Savoury snacks	0.176	0.098	0.008	-0.038	0.349
Fruit	0.266	0.221	-0.218	**0.468***	0.193
Bananas	0.084	-0.149	-0.110	0.154	0.349
Vegetables	-0.006	**0.656***			
Baked beans	0.031	-0.307	-0.005	0.309	**0.574***
Vegetables pies/pastries	0.014	0.221	0.227	0.146	-0.091
Sugar/honey/jam	0.320	-0.023	**0.570***	0.101	-0.017
Biscuits, cakes and pastries	-0.109	0.366	**0.409***	-0.178	0.180
Chocolate	0.087	-0.013	0.205	-0.125	**0.512***
Puddings	0.242	0.314	-0.126	0.000	-0.137
Pulses	0.173	0.339	0.132	**-0.497***	-0.151
Nuts/seeds	0.131	**0.577***	0.128	0.308	0.025

Bold* indicates factor loading ≥0.4 for pattern

4.5 Maternal physical activity

4.5.1 **Physical activity wear time data**

Table 4.17 shows WT data for participants for whom at least three days valid accelerometry data was available at each study visit. Mean daily WT was 1289.0 (IQR 125.0), 1270.5 (IQR 186.6) and 1259.0 (IQR 149.0) minutes in trimesters 1, 2 and 3 respectively.

Table 4.17 Participants with valid WT data at each study visit

	Trimester 1 (n=63)	**Trimester 2 (n=52)**	**Trimester 3 (n=47)**
WT			
Wear periods/day	2 (3) (1-8)	4 [3] (1-13)	4 [3] (1 – 15)
Average daily WT (min)	1289.0 [125.0] (664.0 – 1440.0)	1270.5 [186.6] (650.0 – 1440.0)	1259.0 [149] (651.0 – 1440.0)
Percent wear (%)	89.2 [10.0] (38.10-100.0)	87.4 [16.1] (38.2 – 100.0)	87.4 [12.6] (45.2 – 100.0)
Median [IQR](range)			

As previously reported, compliance with the accelerometry arm of the study was variable in each trimester due to various reasons (Table 4.6). Table 4.18 shows the differences in WT over the course of pregnancy in women who had valid accelerometry data in all three trimesters (n=38). There was a non-significant trend for average daily WT to decrease as pregnancy progressed.

Table 4.18 Participants with valid WT data across all three visits (n=38)

	Visit 1	**Visit 2**	**Visit 3**	**p**
WT				
Average daily WT (min)	1321.0 [135.2])	1306.0 [171.8]	1269.0 [137.5]	0.067
Percent wear (%)	90.8 [9.7]	92.2 [11.4]	88.2 [13.0]	0.057
Median [IQR]				

4.5.2 **Physical activity scoring data**

Table 4.19 shows the scoring data for all participants for whom data was available; decreasing from 63 women to 52 and 47 women in trimesters 1, 2 and 3, respectively.

Table 4.19 Scoring data for participants in each study visit.

	T1 (n=63)	T2 (n=52)	T3 (n=47)
MET Rate	1.7 ± 0.3	1.7 ± 0.2	1.7 ± 0.3
Freedson (1998) bouts			
Mean length of Freedson bouts (min)	16.5 [3.2][b]	16.2 ± 2.1	16.1 ± 3.5
Sedentary Bouts			
Time spent in sedentary bouts/day (min)	347.3 [124.5][b]	304.6 ± 113.9	313.9 ± 104.8
Mean length of sedentary bouts (min)	22.0 {21.3-22.6}[a]	23.0 ± 2.6	22.4 ± 1.9
Sedentary Breaks			
Time spent in sedentary breaks/day (min)	897.7 ± 183.6	927.7 ± 215.4	914.1 ± 133.2
Mean length of sedentary breaks (min)	59.6 [23.9][b]	68.4 [37.1][b]	62.9 [29.7][b]
Freedson Cut Points (% of valid WT)			
Sedentary (0-99 cpm)	45.3 [11.5][b]	44.6 ± 8.8	46.2 ± 9.2
Light (100-1951 cpm)	37.6 ± 5.9	40.7 ± 7.2	38.7 ± 7.6
MVPA (≥ 1951 cpm)	15.9 ± 6.8	14.6 ± 4.9	15.1 ± 5.8
Mean MVPA/day (min)	196.2 ± 72.0	181.4 ± 64.2	186.5 ± 72.3
Step counts			
Mean counts/minute	9.5 ± 2.9	9.0 ± 2.0	8.6 ± 2.1

Mean ± SD
[a]Mean calculated by back-transformation {CI}
[b]Median [IQR]

In order to test for changes in physical activity over the duration of pregnancy, only women with valid accelerometry data in all three trimesters (n=38) could be included in analysis. The only outcome that appears to change significantly across the trimesters is mean step CPM which decreases from 9.6 ± 3.3 steps in trimester 1, to 8.8 ± 2.0 steps in trimester 2, to 8.5 ± 2.1 steps in trimester 3 ($F(2, 23.356) = 3.473$, $p=0.048$;

Table 4.20). However, pairwise comparisons with a Bonferroni adjustment for multiple comparisons do not show any significant difference between trimester 1 and 2 (p= 0.321) or trimesters 2 and 3 (p=0.863), and while the mean difference between trimesters 1 and 3 approaches significance, it does not reach significance (p=0.093). There was a trend for time spent in MVPA to decrease across pregnancy from 207.9 ± 70.6 to 187.3 ± 62.7 minutes to 181.3 ± 68.6 minutes in trimesters 1, 2 and 3, respectively, but this trend did not quite reach significance (p=0.064). There was also a trend for time spent in sedentary activity to increase in trimester 3 (47.6 % (IQR 12.7) compared with trimester 1 (45.4 % (IQR 11.5) and trimester 2 (44.0% (IQR 10.6) but once again, these differences were not significant (p=0.607).

Table 4.20 Scoring data for participants with valid wear data from all three trimesters (n=38)

	T1	T2	T3	p
MET Rate	1.7 ± 0.3	1.7 ± 0.2	1.7 ± 0.3	0.843
Freedson (1998) bouts				
Mean length of Freedson bouts (min)	16.5 ± 2.4	16.4 ± 2.0	15.8 ± 3.5	0.398
Sedentary Bouts				
Time spent in sedentary bouts/day (min)[a]	361.9 [87.6]	341.4 [136.0]	328.9 [156.1]	0.283
Mean length of sedentary bouts (min)	22.2 2.7	22.6 ± 2.3	22.5 ± 1.9	0.591
Sedentary Breaks				
Time spent in sedentary breaks/day (min)	926.8 ± 184.3	934.4 ± 160.6	915.6 ± 123.8	0.817
Mean length of sedentary breaks (min)[a]	61.0 [19.3]	66.9 [22.7]	62.2 [28.8]	0.275
Freedson Cut Points (% of valid WT)				
Sedentary (0-99 cpm)[a]	45.4 [11.5]	44.0 [10.6]	47.6 [12.7]	0.607
Light (100-1951 cpm)	37.2 ± 6.0	39.5 ± 6.4	38.2 ± 6.8	0.076
MVPA (≥ 1951 cpm)	16.5 ± 7.2	14.6 ± 4.4	14.6 ± 5.6	0.119
Mean MVPA/day (min)	207.9 ±70.6	187.3 ± 62.7	181.3 ± 68.6	0.064
Step counts				
Mean counts/minute	9.6 ± 3.3	8.8 ± 2.0	8.5 ± 2.1	0.048

Mean ± SD, RM ANOVA
[a]Median [IQR], Freidman test

4.6 Infant outcomes

Information concerning the delivery of infants was available for 74 participants and is described in Table 4.21. Two participants delivered outside of PHNT, and delivery data from notes was not available for one of these participants. Three infants were born preterm (< 37 weeks gestation) and were therefore excluded from main analysis. Median length of gestation was 275 days and was not significantly different by infant gender.

Table 4.21 Length of gestation at delivery

	All (n=74)	Boys (n=42)	Girls (n=32)	p
Gestation (days)	275 (13.0) [236-292]	275 (12.25) [257-292]	274.5 (13.75) [236-292]	0.428
Gestation (weeks^{+days})	39^{+2} (-) [33^{+5}- 41^{+5}]	39^{+2} (-) [36^{+5} – 41^{+5}]	39^{+2} (-) [33^{+5}- 41^{+5}]	-

Median (IQR) [range], Mann-Whitney U test

A total of 63% of the infants were born by vaginal delivery, while the remaining women delivered via a caesarean section, for various reasons (Table 4.22). Labour onset was spontaneous for 32% of women while the remainder had their labours induced for reasons such as GDM (17%), postdates (7%) or another reason (44%).

Table 4.22 Delivery information (n=71)

	n (%)
Vaginal delivery	**45 (63)**
Spontaneous vertex	40 (56)
Forceps delivery	3 (4)
Ventouse delivery	2 (3)
Caesarean Section	**26 (37)**
CS1 Immediate threat to maternal or neonatal life	3 (4)
CS2 Maternal or foetal compromise	12 (17)
CS4 Delivery timed to suit	11 (16)
Labour Onset	
Spontaneous	**23 (32)**
Induced	**48 (68)**
Induced due to postdates	5 (7)
Induced due to GDM	12 (17)
Other reason	31 (44)
Infant Gender	
Male	41 (58)
Female	30 (42)

Infant anthropometric measurements acquired from hospital notes are presented in Table 4.23, and from the researcher's home visit in Table 4.25. A home visit was not

always possible, especially for women who were lost to follow up, so there is considerably less data available for outcomes measured by the researcher at home (n=58) than for birth weight and delivery data which was obtained from delivery notes by the research midwife (n=74). No differences were observed between boys and girls for any measurements. Mean birth weight was 3497 ± 461g, while mean birth weight z-score was 0.20 ± 0.85. Median head circumference was 35.0cm (IQR 2.0) while mean head circumference z-score was 0.37±1.11.

Table 4.23 Infant anthropometrics by infant sex at delivery

	All	Boys	Girls	p
Birth weight (n=71)				
Birth weight (g)	3497.0 ± 461.0 (2600-4600)	3518.8 ±472.8 (2600 – 4600)	3466.7 ±451.97 (2630-4600)	0.642
Birth weight centile[a]	60.0 [49.0] (11.0-99.3)	51.0 [49.0] (11.0-99.3)	69.0 [46.75] (13.00-98.0)	0.162
Birth weight z-score	0.20 ± 0.85 (-1.21-2.46)	0.10 ± 0.86 (-1.21-2.56)	0.34 ± 0.84 (-1.13-2.04)	0.228
Head Circumference (n=55)				
Head circumference (cm)[a]	35.0 [2.0] (30.0-38.0)	35.3 [2.25] (30.0-38.0)	34.9 [2.0] (32.0-38.0)	0.316
Head circumference centile[a]	67.0 [59.0] (0.1-99.8)	69.0 [61.50] (0.1-99.4)	64.0 [49.0] (11.0-99.80)	0.595
Head circumference z score	0.37 ± 1.11 (-2.72-2.93)	0.28 ± 1.17 (-2.72-2.53)	0.48 ± 1.05 (-1.22-2.93)	0.499

Mean ± SD (range), independent samples t test
[a]Median [IQR] (range), Mann-Whitney U test

No infants were born SGA and just 6 infants were classified as LGA. A total of ten infants were classified as macrosomic, 7 in Class I (BW ≥ 4000g and < 4500g) and 3 in

Class II (BW ≥ 4500g), Table 4.24. The median age of the infant at the home visit was 5 days and ranged from 2-14 days, based on participant availability. Mean crown-heel length was 50.8 ± 2.1cm and mean crown-heel length z-score was -0.10 ± 0.10.

Table 4.24 Infant birth size characteristics (n=71).

Birth weight (BW) for Age	**n (%)**	**Macrosomic Class**	**n (%)**
SGA Infants (<10th centile)	0 (0)	Not macrosomic (<4000g)	61 (86)
AGA Infants (≥10th and <90th centile)	65 (91.5)	Class I (≥4000g <4500g)	7 (10)
LGA Infants (≥90th centile)	6 (8.5)	Class II (≥4500g <5000g)	3 (4)

Table 4.25 Anthropometrics from infant home visit.

	All (n=58)	**Boys (n=30)**	**Girls (n=28)**	**p**
Age of infant				
Age (days)[a]	5.0 [3.25] (2.0-14.0)	5.0 [3.00] (2.0-14.0)	5.50 [4.0] (2.0-12.0)	0.706
Crown-heel length	**n=56**	**n=29**	**n=27**	
Crown-heel length (cm)	50.8 ± 2.1 (45.5-55.0)	51.0 ± 2.4 (45.5-55.0)	50.65 ± 1.78 (48.0 – 54.5)	0.603
Crown-heel length centile	46.9 ± 28.9 (2.0-95.0)	42.0 ± 30.9 (2.0-95.0)	52.2 ±26.2 (12.0-94.0)	0.163
Crown-heel length z-score	-0.10 ± 0.93 (-2.01-1.6)	-0.28 ± 1.02 (-2.01-1.60)	0.09 ± 0.80 (-1.20-1.52)	0.143
Body composition	**n=56**	**n=29**	**n=27**	
AC (cm)[a]	10.00 [1.5] (8.0-12.0)	10.0 [0.85] (8.0-11.5)	10.0 [1.50] (8.0-12.0)	0.855
Triceps SFT (mm)	6.7 ± 1.8 (3.4-10.8)	6.7 ± 1.8 (4.5-10.8)	6.8 ± 1.8 (3.4-10.2)	0.830
UFE (cm^2)	334.4± 108.2 (153.0-586.5)	333.3 ± 107.5 (180.0 – 550.8)	335.6 ± 110.9 (153.0 – 586.5)	0.939
UME (cm^2)	445.5 ± 105.1 (221.3-695.9)	444.1 ± 95.5 (255.8 – 621.2)	438.6 ± 16.3 (221.3 – 695.9)	0.847

Mean ± SD (range), independent samples t test
[a]Median [IQR] (range), Mann-Whitney U test

4.7 Discussion

4.7.1 **Recruitment of participants**

Although 838 women were identified as meeting study inclusion criteria, of these, only 75 women were enrolled. As shown in Table 4.1, the majority of women (516 women, 62%) were not approached, which was unavoidable due to the nature of a study conducted by a single researcher who was responsible for recruitment, enrolment and data collection throughout the follow-up period. A further 79 women (9%) could not be approached as they did not meet inclusion criteria. Of the 242 women who were approached by the researcher at their scan, 140 women (58%) declined the invitation to participate. This figure is slightly higher than that observed in a considerably larger prospective cohort study amongst women with a BMI ≥ 30 kg/m^2 set in Liverpool, UK (Narayanan *et al.*, 2016). They reported that 47% of women meeting inclusion criteria 'did not consent or were not approached,' although the proportions of women who 'did not consent' or 'were not approached' were not reported. A total of 81% of eligible women declined to participate in the UK Pregnancies Better Eating and Activity Trial (UPBEAT), however, although similar data regarding GWG, incidence of GDM and infant birth size was collected, this was also an intervention study which could explain the higher rate of refusal as the burden placed on participants was greater (Poston *et al.*, 2015).

Women were not required to give a reason for their refusal to participate in the study, and the majority did not (89%). However, of those who did give a reason, 13% said they did not have time, and 2% said they were unhappy with the measurements that

would be taken. Other UK cohort studies do not appear to have reported reasons for non participation, although work exploring women's reasons for non-attendance at a UK weight management service during pregnancy suggested that time commitment, feeling unwell during pregnancy and 'not wanting to focus on one's weight during pregnancy' were the most common reasons for non-attendance (Olander and Atkinson, 2013) with similar themes identified in a similar study in Australia (Davis *et al.*, 2012).

With respect to the original sample size calculation, 82 women were required, and in order to allow for up to 15% attrition, a target of 97 women for recruitment was set. This target was met, however, of the 102 women who agreed to participate, 26 did not keep their first study appointment so 75 consented to take part in the study and were therefore enrolled, which brought the total number to women with study data to 92% of the original target.

4.7.2 **Retention of participants**

Data was collected at the end of the first trimester at study visit 1 on all of the 75 women who enrolled in the study, with 10 women (13%) lost to follow up between visit 1 and 2, and a further 2 women lost between visit 2 and 3 (16%). Infant data was available from the notes of 74 women and the researcher made visits to 58 infants (77%) in the days following delivery.

Of the women who enrolled in the study, attrition was 16%, which is similar to that of the control arm of the UPBEAT study which placed a similar burden on participants with an attrition rate of 20% (Poston *et al.*, 2015). However, if including the women

who originally agreed to participate in the current study, 38 of 102 women failed to complete the study, which equates to an attrition rate of 38%, considerably higher than that observed in the literature. The high number of women withdrawing from the study between recruitment and study visit 1 was unexpected. The researcher can only hypothesise that women perhaps felt obliged to accept the invitation to participate when approached personally in antenatal clinic, but more able to decline once out of the hospital by text or phone message, or by simply not keeping the first appointment. Even amongst women who were not lost to follow-up, compliance with the different aspects of the study varied considerably and full anthropometric, diet and physical activity in all three trimesters, plus infant anthropometry was obtained for 34 women, just 45% of the original cohort enrolled, and 33% of those originally recruited. Anthropometric data was collected at the end of all three trimesters for 57 women (76%) which was considerably higher than the proportion of consenting women who had weights recorded at all 3 time-points in the study (51%) conducted by Narayanan et al. (2016). Higher adherence in the present study is possibly due to the personal approach of just one researcher making personal appointments with women, while larger studies such as Fit for Birth (Narayanan et al., 2016) and UPBEAT (Poston et al., 2015) require multiple study staff to obtain measurements.

Physical activity data, as assessed by accelerometry at each study visit, was collected for 63 (84%), 52 (69%) and 47 (63%) women at the end of trimesters 1, 2 and 3, respectively. These figures exceed those observed in a pilot study of 189 women in the UPBEAT study at three similar time-points in pregnancy: 77%, 42% and 30%,

respectively (Hayes *et al.*, 2015). Compliance with the four-day diet diary was better than compliance with accelerometry with 67 (89%), 58 (77%) and 52 (69%) women complying with this arm of the study following each study visit. Diet was assessed at baseline and at the end of the second trimester in the UPBEAT study, with 88% and 79% of women in the control group completing FFQs at each time-point respectively, which was similar to compliance in the present study (Poston *et al.*, 2015).

Reasons for non-compliance with the diet and physical activity arms of the study were varied and included: women being unwilling or unable to wear an accelerometer due to discomfort or to the nature of their occupation, accelerometer failure, insufficient accelerometer WT and lost or incomplete diaries. A further 4 women delivered their babies before study visit 3 was completed, so were missing all data for the end of their third trimester.

Higher than expected study attrition, and non-compliance with the diet and physical activity arms of the study has resulted in data being collected on less women than required from the original sample size calculation. This has been considered throughout data analysis, and achieved power has been calculated and reported where appropriate.

4.7.3 **Description of the participants**

The age of women recruited ranged from 19 to 40 years, with a mean age of 29.8 years. This was similar, although slightly younger than the mean age of 30.3 and 30.4 years of mothers of all live births in England and Wales in 2015 and 2016, respectively (Office for National Statistics, 2017b). However, the present study excluded women

younger than 18 years and older than 40 years who would have been included in the national estimates of average age at childbirth.

Obstetric history of the women varied considerably and 37% of participants were nulliparous, which compares favourably with national data from the study period where 39% and 41% of live births were first births in 2015 and 2016, respectively (Office for National Statistics, 2017b).

The median Index of Multiple Deprivation decile for the cohort was 4.0 which is the same as the median decile for the 161 LSOAs in Plymouth (Department for Communities and Local Government, 2015). This suggests that the cohort was representative of the city, which also has a median decile of 4.0 and is ranked 69th most deprived out of 326 local authorities (Plymouth City Council, 2016).

Eight women, 11% of the cohort, reported an intention to continue smoking during their pregnancy, and this was based entirely on self-report. This is similar to the figure of 11.7% of women smoking at time of delivery reported in Plymouth in 2016-2017, which is slightly higher than the figure reported for women in England of 10.7% (Public Health England, 2018). Smoking during pregnancy is associated with a number of adverse outcomes, including increased risk of miscarriage, premature birth, LBW and SGA (Meyer and Tonascia, 1976). However, as the proportion of women reporting smoking appeared to be similar to the general population, and many women under-report their smoking status (Walsh *et al*., 1996), it was not felt appropriate to remove these women from analysis, as this would reduce the sample size of the population.

Mean BMI at booking was 32.7 kg/m^2, with 62 (83%) women falling into Class I obesity, with a BMI ≥ 30 but <35 kg/m^2, and the remaining 13 (17%) women falling into Class II, with a BMI ≥35 but <40 kg/m^2. Although all women with a BMI ≥30 and <40 kg/m^2 were eligible to participate, it should be noted that other research studies were being conducted amongst women with a BMI ≥35 kg/m^2 which reduced the number of women with Class II obesity who could be approached. From the researcher's perspective, women with Class II obesity also seemed to be more reluctant to participate in the study, although data could not be recorded.

4.7.3.1 Maternal gestational weight gain

As expected, maternal weight generally increased as pregnancy became more advanced and GWG varied considerably between participants. In trimester 1, mean GWG was 0.9 ± 3.2 kg and ranged from GWL of 9.0kg to GWG of 12.4kg. Trimester 1 GWG was based on the difference between booking weight, recorded by the participant's midwife, and the weight measured by the researcher at study visit 1. Trimester 1 GWG should therefore be interpreted with caution, as the gestation at which participants booked varied considerably between women (data not available), the scales used to measure weight will have varied between booking locations, and their calibration history is not known. Although mean GWG in trimester 1 falls within the IOM recommended guidelines of 0.5-2 kg GWG for all women, irrespective of BMI, these measurements are likely subject to random error and there is considerable individual variation.

In order to adjust for varying gestation at each study visit, mean rate of GWG during trimester 2 was calculated to be 0.33 ± 0.23 kg/week, and ranged from -0.31–0.87 kg/week. This observed rate of trimester 2 GWG is similar to that observed in the US Project Viva cohort of women with a BMI ≥ 30 of 0.31 kg/week, which ranged from -0.41 to 0.97 kg/week (Walter *et al.*, 2015). Based on IOM recommendations for women to gain 0.17-0.27 kg/week in trimesters 2 and 3, just 10 women in the present study (15%) were gaining within IOM guidelines, while 38 women (59%) exceeded recommendations and 17 women (26%) gained below recommendations.

Mean rate of GWG during trimester 3 was 0.29 ± 0.40 kg/week which was 0.04kg/week less than in the previous period, but once again there was individual variation, with rate ranging from -0.50-1.26 kg/week. The observed rate of trimester 3 GWG is lower than the rate observed amongst women in Project Viva of 0.39 kg/week with a range of -0.45-1.00 kg/week (Walter *et al.*, 2015). Just 3 women (5%) gained within, 31 women (54%) exceeded and 23 women (40%) gained below IOM guidelines.

In order to assess total GWG over pregnancy, the difference between study visit 1 and study visit 3 was calculated which does not take GWG prior to study visit 1, nor GWG after study visit 3 into account, so rate of GWG was used for analysis. Mean total rate of GWG was 0.32 ± 0.26 kg/week and ranged from -0.28-0.91 kg/week. The Project Viva study did not report mean rate of GWG during trimesters 2 and 3, as they collected GWG earlier in pregnancy and were able to include trimester 1 in their total GWG rate. Project Viva data is therefore not comparable to the present study's 'total rate of GWG' as trimester 1 GWG tends to start more slowly and is not linear

throughout pregnancy (Kleinman *et al.*, 2007). It should also be noted that Project Viva included all women with a BMI $\geq$ 30 kg/m^2, and therefore some women included in their analysis may have had a BMI $\geq$ 40 kg/m^2 and therefore have exhibited different patterns of GWG when compared to women in the present study with Class I or Class II obesity. Durie et al (2011) reported rate of trimester 2 and 3 GWG in lbs, for Class I and Class II women with obesity, which converts to approximately 0.45 and 0.36 kg/week, respectively. Just 8 women in the present study (14%) gained within IOM recommended ranges of GWG, with 33 women (58%) gaining in excess and the remainder gaining below guidelines. Durie et al (2011) reported slightly higher adherence to IOM recommendations amongst Class I and Class II women with obesity of 14.4 and 18.3%, respectively, while 70.2 and 57.5% gained in excess of guidelines, respectively.

4.7.3.2 Maternal body composition

Percentage body fat was estimated from skinfold measurements taken from the triceps, biceps and subscapular using an equation previously validated in pregnant women with overweight or obesity (Kannieappan *et al.*, 2013) that was later used by the authors to report outcomes from the LIMIT randomised trial in Australia (Dodd et al., 2015). Mean percentage body fat in the present study was 40.3 ± 4.5% at study visit one, which is similar, although slightly higher, than that observed amongst the control arm of the LIMIT trial of 37.7 ± 7.5 %. Mean biceps, triceps and subscapular SFT in the present study were 18.9 (95% CI 17.6 – 20.3), 29.6 ± 5.2, and 34.2 ± 7.5 mm, respectively, which once again, are similar to values observed in the LIMIT trial: 17.4 ±

6.9, 28.4 ± 7.4 and 29.4 ± 9.7 mm, respectively. Values observed from LIMIT had a larger degree of variation, which is to be expected, as despite having a similar mean BMI to the present study, the LIMIT trial was conducted amongst women with overweight and Class I – III obesity, while the present study included women with Class I and Class II obesity only. Mean early pregnancy FM in the present study was 35.8 kg (95% CI 34.4 – 37.2), which is similar to that observed by Soltani and Fraser (2000) amongst participants with obesity (mean BMI 34.5 ± 3.5 kg/m^2) of 36.1 ± 5.9 kg who used a different equation, with the addition of suprailliac and mid-thigh skinfold measurements, to estimate body fat in early pregnancy.

MUAC was 35.2 ± 2.7, 34.8 ± 2.8 and 34.3 ± 3.0 cm at visits made to participants at the end of each of the three trimesters respectively in the present study. MUAC was also reported at three time-points in the UPBEAT trial as 36.8 ± 4.0, 36.9 ± 4.2 and 36.6 ± 4.1 cm at weeks 15-18, 27-28 and 34-36, respectively, while the LIMIT trial reported mean MUAC in early pregnancy as 35.4 ± 4.4 cm.

Analysis revealed that changes in rate of FM, but not FFM, accrual were significantly different between women gaining below, within and in excess of IOM GWG guidelines. For GWG during trimester 2, trimester 3 and during trimesters 2 and 3 combined, women gaining in excess of IOM guidelines exhibited significantly higher FM accrual than women gaining below the guidelines. In trimester 2, and trimesters 2 and 3 combined, women gaining in excess of IOM guidelines also exhibited significantly greater rates of FM accrual than women gaining within IOM guidelines. There were no significant differences between IOM groups for rate of FFM accrual at any time-point

of pregnancy, suggesting that accrual of FFM is consistent between groups. Similarly, Widen and colleagues (2015) observed greater gains in maternal FM for women gaining medium and high rates of GWG in the second trimester, and high rates of GWG in the third trimester, compared with women gaining low rates of GWG; although rate of GWG group was determined based on tertiles of GWG in the study population rather than using IOM guidelines to group women. Berggren et al. (2016) showed that women gaining in excess of IOM guidelines gained significantly greater FM than women gaining both within and below guidelines. While FFM correlated with total GWG, no differences in FFM were observed between women gaining in excess and within guidelines, although unlike the present study, there was a significant difference between change in FFM amongst women gaining in excess and below guidelines.

4.7.3.3 Gestational diabetes mellitus

Of the total study population (n=75), 19 women (25%) were diagnosed with GDM according to PNHT diagnostic criteria (fasting plasma glucose level ≥ 5.3 mmol/litre or a 2-hour plasma glucose level of ≥7.8 mmol/litre). OGTT results were not available for 3 women, while 53 women (71%) had a negative result. The proportion of women diagnosed with GDM in the present study (25%) is very similar to observations made amongst women in the 'standard care' arm of the UPBEAT study of whom 26% were diagnosed with GDM (Poston *et al.*, 2015). These findings are in contrast to those observed in the 'Fit for Birth' cohort amongst women with BMI ≥30 and <40 kg/m^2, where just 3.6% of women were diagnosed with GDM (Narayanan *et al.*, 2016). These differences are likely due to differences in diagnostic criteria for GDM between

studies. For example, Poston et al (2015) used IADPSG diagnostic criteria for GDM which diagnoses GDM if fasting plasma glucose level ≥ 5.1mmol/litre or 2-hour plasma glucose level ≥8.5 mmol/litre (International Association of Diabetes and Pregnancy Study Groups Consensus Panel, 2010) while the Fit for Birth cohort used WHO diagnostic criteria (fasting plasma glucose ≥7.0mmol/litre, litre or a 2-hour plasma glucose level of ≥7.8 mmol/litre) (World Health Orgnanisation, 1980). It is therefore difficult to make comparisons between studies with regards to GDM outcomes and there is a move in the literature towards reporting GDM using IADPSG criteria in order to make local, national and global comparisons.

No differences in maternal characteristics such as maternal age, parity or deprivation, as defined by the Multiple Index of Deprivation, were observed between women who developed GDM and those who did not (Table 4.11). Previous research has identified advancing maternal age, parity, family history of diabetes and ethnicity as risk factors for GDM (Berkowitz *et al.*, 1992; Di Cianni *et al.*, 2003). Data on family history of diabetes was not collected, and only women who identified as 'white Caucasian' were recruited due to the nature of the population in Plymouth and number of women required for power to examine ethnic differences in outcomes. The present study also restricted the age at which women could participate to 40 years which may have affected the prevalence of GDM observed. Previous research conducted within Plymouth identified advancing maternal age, but not deprivation, as a risk factor for GDM in a large sample of women (n=3933) (Janghorbani *et al.*, 2006).

4.7.4 **Maternal diet**

4.7.4.1 Dietary intakes

Women were asked to complete a four-day food diary following each study visit, with 66, 58 and 52 women completing a diary at study visits 1, 2 and 3, respectively. As expected, daily EI tended to increase as pregnancy advanced from 1766 ± 433 kcal to 1829 ±418 kcal to 1910± 452 kcal in trimesters 1, 2 and 3, respectively, suggesting a mean increase in energy of 144kcal across pregnancy. These values suggest that food and EI is likely to have been under-reported by the cohort as estimated average requirements (EARs) for energy are 2175 kcal/day for women aged 19-34 years, and 2103 kcal/day for women aged 35-44 years plus an increment of 191 kcal/day in the third trimester for all women regardless of age (Scientific Advisory Committee on Nutrition, 2011). It is possible that women either changed their eating habits, because they knew they were being observed, known as the Hawthorne effect (Parsons, 1974), or that they consciously or unconsciously under-reported their actual food intake (Macdiarmid and Blundell, 1998). McGowan and McAuliffe (2012) suggest that a Goldberg ratio <0.9 (Goldberg *et al.*, 1991) should be used as a sign of definite underreporting amongst pregnant women at the end of their first trimester. However, although women with known hyperemesis were excluded from their study, nausea and vomiting was not closely monitored, which could thus explain low EI in some participants (McGowan and McAuliffe, 2012). The proportion of women classified as 'definite under-reporters' in the present study was 26, 28 and 21% in trimester 1, 2 and 3, respectively, while pregnancy sickness was reported amongst 80% of women in

trimester 1. Although information was collected on the presence and nature of pregnancy sickness, women's' experiences of pregnancy sickness varied with some women reporting an increased food intake, others reporting a change in the types of foods consumed, others reducing their food intake at specific times of the day, and some women eating very little. Although data was re-analysed to exclude 'definite under-reporters' (Appendix 9) it has not been included in the main analysis as without the use of biomarkers in the present study, it is not possible to identify with certainty which women under- reported their food intake and which women experienced pregnancy sickness-related changes to their food intake. Under-reporters will have lower intakes of macronutrients, so macronutrients are expressed as a percentage of energy, rather than as absolute intakes (g/day) in order to attempt to partially address this limitation and allow for comparison between women in the present study. This will not, however, address any macronutrient- or food-specific underreporting (Macdiarmid and Blundell, 1998) and may lead to an imbalance or reciprocal relationship such as the 'sugar-fat see-saw' observed in the general population whereby the percentage energy obtained from one, is inversely associated to the other (Sadler, McNulty and Gibson, 2015).

All women received an OGTT at approximately 28 weeks gestation in order to test for the presence of GDM, which coincided with the approximate timing of study visit 2. In order to take account of changes that women diagnosed with GDM may have made to their diets before, during or after study visit 2, women with GDM were excluded from analysis. A total of 34 women without GDM completed diaries following all three study

visits and repeated measures ANOVA was performed in order to examine for any differences between trimesters (Table 4.15), which were not observed for energy, nor the proportion of energy coming from any macronutrient. Mean daily EI was not significantly different between trimesters at 1870 ± 410 kcal, 1840 ± 358kcal and 1975 ± 413 kcal in trimesters 1, 2 and 3, respectively. As stated above, it is likely that this is an underestimation of EI, and the standard deviation is large across all three trimesters. The UPBEAT study observed mean daily EIs from FFQs of 1864 ± 621kcal and 1793 ± 550 kcal at 15-18^{+6} weeks gestation and 27-28^{+6} weeks gestation, respectively, in the standard care arm of their study, which are also considerably less than the EARs for women (Poston *et al.*, 2015). Conversely, mean EI assessed from 7 day food diaries administered in early pregnancy amongst women in Portsmouth, UK was slightly higher at 2031 ± 15.6SE kcal/day, (Mathews and Neil, 1998), although this cohort included women of all weights, so may have reported their food intake in a different manner to women with obesity.

There was a non-significant trend for the proportion of energy from carbohydrate to decrease from trimester 1 (53.7 ± 6.7%) to trimester 2 (52.1 ± 4.8%) to trimester 3 (51.3 ± 4.9%). Mean proportion of dietary energy from carbohydrate in all three trimesters was therefore similar to the SACN recommendations that approximately 50% of dietary energy should come from carbohydrate (Scientific Advisory Committee on Nutrition, 2015). The values observed in the present study are slightly higher than those observed by Mathews & Neil (1998) in early pregnancy and Poston et al. (2015) in early and mid-pregnancy of 47.3%, 49.4% and 48.6%, respectively. It is likely that

carbohydrates intake is higher amongst the present cohort due to high intakes of foods containing added sugars. Mean daily proportion of energy from total sugars was 21.1 (95% CI 19.5 -22.7) %, 20.7 ± 7.2 % and 20.1 ± 7.2 % in trimesters 1, 2 and 3, respectively. However, it is not possible to compare these figures to the recommendation that free sugars should not exceed 5% of dietary energy (Scientific Advisory Committee on Nutrition, 2015) as total sugars includes sugars occurring naturally in foods such as milk and fruit are included within the definition of 'total sugars.' Neither Mathews & Neil (1998) nor Poston et al. (2015) reported the proportion of energy from total sugars so findings from the present study cannot be compared to any studies with a similar population.

Total energy intake from fat remained fairly stable throughout pregnancy, and was similar to the recommendation to obtain 35% of food energy from fat (Department of Health, 1991) while total energy from saturated fat tended to increase as pregnancy progressed: 12.4 ± 2.2%, 13.0 ± 2.4% and 13.7 ± 2.8%, respectively, which did not quite reach significance. Charnley et al. (2015) observed a statistically significant increase in intakes of total, saturated and monounsaturated fats in their observational study amongst women with obesity in Liverpool, UK. The authors hypothesised that this was due to a decrease in diet quality and increase in convenience foods as pregnancy progressed. The proportion of energy coming from saturated fat in the present study is considerably higher than the recommendation that no more than 11% of energy should come from saturated fats (Department of Health, 1991) and are also similar to

the values observed by Poston et al. (2015) in early and mid-pregnancy of 12.7 ± 3.0% and 13.1 ± 3.0%, respectively.

Mean energy from protein was at, or slightly higher than recommendations that 15% of food energy is obtained from protein (Department of Health, 1991) at 15.3 ± 2.9%, 16.0 ± 2.8% and 16.2 ± 2.4% in trimesters 1, 2 and 3 respectively. These values are quite considerably less than those observed by Poston et al. (2015) of 19.7 ± 4.4% in early and 20.1 ± 4.0% in mid-pregnancy, but similar to values observed in early and late-pregnancy by Charnley and colleagues (2015; 15.7% and 16.2%, respectively). Differences in observed dietary intakes across pregnancy between studies are likely due to methodological and population differences. Particularly important to consider is that women in the current study were all of white Caucasian origin, while other studies included women of different ethnicities, whose diets may have been different, and thus influenced nutrient intakes.

4.7.4.2 Dietary patterns

Five dietary patterns were identified from first trimester diet diaries via PCA. Although dietary data was collected from participants in trimesters 2 and 3, as some participants changed their diets in response to GDM diagnosis, and compliance with diet diaries decreased as the study progressed, it was not felt appropriate to derive dietary patterns from this data. However, it should be acknowledged that 80% of the cohort reported some experience of pregnancy sickness in their first trimester, and thus, the dietary patterns obtained from the present study are likely to have been influenced by

pregnancy sickness, and may not have persisted into the second or third trimesters if symptoms of pregnancy sickness reduced, as they did for the majority of women. The third dietary pattern, which was characterised by high intakes of white bread, butter, added sugar, baked potatoes, cakes and biscuits and could perhaps be deemed similar to 'snack' patterns described in other dietary patterns studies during pregnancy (Okubo *et al.*, 2012; Coelho *et al.*, 2015; Flynn *et al.*, 2015). The remaining patterns were not distinct from each other, for example, pattern 1, characterised by high intakes of dairy foods (milk, cheese and yoghurt), wholemeal cereals, white fish or seafood and roast potatoes, and low intakes of chips and processed meat and pattern 2, characterised by high intakes of poultry, vegetables, nuts and seeds, rice, red meat and sugar free soft drinks, could both be defined as 'healthy' or 'prudent,' as described by other studies (Radesky *et al.*, 2008; Knudsen *et al.*, 2013; Starling *et al.*, 2017). Patterns 4 and 5 were high in eggs and fruit, and baked beans, pasta or noodles and chocolate, respectively, and did not fit into any previously described patterns. The lack of distinct dietary patterns is perhaps not surprising from the present cohort due to the small sample and the homogenous group of white Caucasian women all living in Plymouth, UK. Other studies, with more diverse study populations, particularly UPBEAT (Flynn et al., 2016), observed associations between dietary patterns and social and demographic factors, such as ethnicity and level of education, which could not be accounted for the in present study. As discussed previously, methods of dietary data collection and statistical analysis used for deriving *a posteriori* dietary patterns vary

considerably between studies, which makes comparison difficult particularly as the foods consumed varied considerably across the populations studied.

It is also likely that some women under-reported their dietary intake, and whether this was systematic under-reporting of portion sizes, particular groups of foods, or of all foods, could not be determined. However, if present, under-reporting is nonetheless likely to have had an impact on the dietary patterns identified in the current study and should also be considered a limitation.

4.7.5 **Maternal physical activity**

The number of women for whom physical activity data was available decreased as pregnancy advanced from 63 to 52 to 47 women in trimesters 1, 2 and 3, respectively. Only 38 women (51%) completed at least 3 days with >500 minutes accelerometry in all three trimesters. Other UK studies have observed declines in compliance across pregnancy (Rousham, Clarke and Gross, 2006; McParlin *et al.*, 2010). Amongst women who completed accelerometry in all three trimesters, there was a trend for average daily WT to decrease from 1289.0 (IQR 5.0) to 1270.5 (IQR186.6) to 1259.0 (IQR 149.0) minutes/day, although this did not quite reach significance. McParlin et al. (2010) observed significant decreases in median recorded time between trimesters 1 and 2 (780.0 (IQR 113.0) vs. 742.0 (IQR 107.0) minutes/day, p=0.018, n=26) and between trimesters 1 and 3 (817.0 (IQR 79.0) vs. 778.0 (IQR 113.0) minutes/day, p=0.019, n=21). Median WT in the present study is considerably higher than that observed in the study conducted by McParlin et al. (2010) and median WT observed amongst pregnant women with overweight and obesity in another UK study (821.8 (IQR 115.3)

minutes/day; (Kinnunen *et al.*, 2011), which is a strength of the present study. Women in the present study were encouraged to wear the accelerometer continuously during 4 days of accelerometry data collection, which could explain the increase in observed WT, as women in the other studies were instructed to wear the accelerometer during waking hours only. A recent study amongst participants in NHANES suggests that wear time < 720 minutes/day underestimates step count and time spent in each physical activity category, and studies achieving wear times less than this should be interpreted with caution (Herrmann *et al.*, 2014).

With regards to physical activity scoring data, the only significant change across pregnancy was a decrease in mean step CPM from 9.6 ± 3.3 to 8.8 ± 2.0 to 8.5 ± 2.1 steps per minute in trimesters 1, 2 and 3, respectively. In contrast, mean time spent walking per week increased between 15-18 weeks and 27-28 weeks gestation in the control arm of the UPBEAT trial (Poston *et al.*, 2015). The proportion of time spent in sedentary, light or MVPA did not appear to change significantly between trimesters in the present study. There was a trend for time spent in MVPA to decrease as pregnancy progressed from 207.9 ± 70.6 minutes to 187.3 ± 62.7 minutes to 181.3 ± 68.6 minutes in trimesters 1, 2 and 3, respectively, although this trend did not quite reach significance (p=0.064). Data from the intervention and control arms of the UPBEAT study was combined and observed a statistically significant decrease in MVPA between early (39.0 (IQR 27.2) minutes/day) and mid pregnancy (34.5 (IQR 19.6) minutes/day) and early and late pregnancy (23.3 (IQR 20.0) minutes/day; (Hayes *et al.*, 2015). Minutes spent in MVPA in the present study are considerably higher than those

observed by Hayes et al. (2015), those observed by other studies during pregnancy (Kinnunen *et al*, 2011; Ruifrok *et al*, 2014) and the UK physical activity guidelines which recommend ≥ 150 MVPA per week (Department of Health and Social Care, 2010). These differences in findings could be due to differences in WT, which was considerably higher in the present study than in others. Differences in accelerometry methodology could also explain these differences, although both the present study and Kinnunen et al. (2011) used a 60-second epoch length for analysis and Freedson cut-points (Freedson, Melanson and Sirard, 1998). Hayes et al. (2015) also used Freedson cut-points, but did not report epoch length, while Ruifrok et al (2014) used a 60-second epoch but alternative cut-points. Accelerometers were wrist-worn in the present study, waist-worn in Ruifrok et al. (2014) and Kinnunen et al. (2011), while site of accelerometer attachment was not reported by Hayes et al (2015). Previous studies have suggested a moderate correlation between activity assessed by wrist- and hip-worn accelerometers (Kamada *et al.*, 2016; Scott *et al.*, 2017). However, variations in physical activity outcomes have been shown to vary by wear location by up to 41% and up to 52% across data processing techniques in a recent comparison study (Kerr *et al.*, 2017), suggesting that comparisons between studies should be made with caution.

4.7.6 **Infant outcomes**

4.7.6.1 Delivery information

Median length of gestation amongst the 74 women for whom delivery data was available was 39 weeks + 2 days (IQR 1.9 weeks), with three infants born preterm (<37 weeks gestation). Median gestational age was similar to that observed amongst

women in the control arm of the UPBEAT trial (39.5 ± 2.4 weeks). Of 45 infants born by vaginal delivery (63%), 40 were unassisted (56% of total deliveries), while 7 women underwent an operative vaginal delivery (10%). The figures are similar to those observed by Poston et al. (2015) of 63%, 52% and 11% of total births, respectively in the control arm of their study. The remaining 26 women in the present study had a caesarean section (37%), of which 15 were emergency (21% of total deliveries) and 11 were elective (16%), which once again, is similar to observations amongst women in the control arm of UPBEAT of 36%, 18% and 18%, respectively.

4.7.6.2 Infant birth size

The mean birth weight observed in the present study (3497 ± 461g) compares favourably with that reported in the standard care arm of the UPBEAT trial of (3450 ± 560g; Poston et al., 2015) and with that observed in the Australian Collaborative Trial of Supplements (ACTS) trial (3476 ± 631g; Athukorala, Rumbold, Willson, & Crowther, 2010). Mean birth weight z-score was 0.20 ± 0.85 in the present study, which was not reported in the UPBEAT trial, but was reported in the ACTS trial as 0.16 ± 1.08, although based on Australian birth weight charts (Roberts and Lancaster, 1999) and with the Treatment of Obese Pregnancy (TOP) study as 0.21 ± 1.2, which was based on Danish data (Carlsen *et al.*, 2014). Mean head circumference in the present study, UPBEAT trial and ACTS trial was 35 (IQR 2) cm, 34.7 ± 1.8 cm and 34.7 ± 1.9cm, respectively, while birth length was 50.8 ± 2.1 and 50.5 ± 2.9 in the present study and ACTs trial, respectively, and not reported for UPBEAT participants.

Of 71 term infants, 10 infants (14.1%) were born weighing ≥4.0kg, and were classified as macrosomic. This is considerably higher than the proportion of infants born weighing ≥4.0kg in both England and the South West region in 2016 of 10.7% and 12.4%, respectively (Office for National Statistics, 2017a). This is not surprising as these national statistics came from the general population, while the present cohort of women all had obesity, which is a well-documented risk factor for macrosomia (Gaudet, Ferraro and Wen, 2014). However, the proportion of infants defined as macrosomic was similar to the rate of 13.9% observed amongst participants with obesity in the UPBEAT trial (Poston *et al.*, 2015), although considerably higher than the prevalence of macrosomia of 10.3 % and 7.0 % amongst women with Class I and Class II obesity, respectively, in the Fit for Birth study in Liverpool, UK (Narayanan *et al.*, 2016). Based on British 1990 birth weight centiles (Freeman *et al*, 1995), 6 infants (9%) were classified as LGA with a birth weight >90th percentile, which is considerably lower than observed in the UPBEAT trial (11%).

Mean infant triceps SFT was 6.7 ± 1.8 mm which was considerably higher than that observed in the UPBEAT trial of 5.3 ± 1.6 mm (Poston *et al.*, 2015). However, the method employed to measure infant SFT was not documented for the UPBEAT trial, so methods could have varied, and while just one researcher collected non-routine infant anthropometric data in the present study, multiple researchers across multiple research-sites were involved with the collection of UPBEAT data. Other studies conducted outside of the UK report mean infant triceps SFT of 4.4 ± 1.0 mm (maternal BMI ≥ 25.0 kg/m^2) in a USA prospective cohort study (Sewell, Huston-Presley, Super, &

Catalano, 2006) and 5.41 ± 144 mm in the control arm of the LIMIT randomised controlled trial in Australia (Dodd et al., 2016). A slightly higher mean value amongst newborns in the control arm of the Irish ROLO study was observed of 7.07 ± 1.5mm, although participants in this study had previously had a macrosomic baby and mean birth weight was considerably higher amongst infants in this study 4055 ± 434 g (Donnelly *et al.*, 2014). Median infant MUAC in the present study was 10.0 (IQR 1.5) cm, which was lower than mean MUAC observed amongst infants born to control mothers in the LIMIT trial of 11.18 ± 1.1 cm.

4.8 Conclusion

The number of women recruited into the present study met the original target based on the sample size calculation plus allowance for 15% attrition. However, greater than expected attrition between recruitment and first study visit, and further attrition as the study progressed has resulted in data being available for less women than required based on the original power calculation, especially for data collected in the last trimester and for diet and physical activity data. The present study is therefore small compared to others, as further recruitment could not occur due to lack of further time and resources available.

However, the women recruited to participate in the present study appear to be demographically similar to women nationally, and many maternal and infant outcomes, with the exception of physical activity, appear to be similar to those reported in other UK studies amongst women with obesity.

Chapter 5 **Analysis of data**

The research project sought to answer the following three primary research questions. Data relating to these research questions is presented over the following pages, split by research question.

1. **How does diet affect maternal and infant outcomes?**
2. **How does physical activity affect maternal and infant outcomes?**
3. **Does the timing and composition of GWG affect infant birth weight and adiposity?**

5.1 How does diet affect maternal and infant outcomes?

5.1.1 Diet and gestational weight gain

There was no significant relationship observed between trimester 1 GWG and mean EI or proportion of energy from the main macronutrients ($p>0.05$) as shown in Table 5.1.

Table 5.1 Pearson correlations for Trimester 1 GWG and dietary intake, n=66

	Energy, kcal	% energy CHO	% energy sugar	% energy fat	% energy protein
Trimester 1 GWG, kg	0.146	-0.067	-0.115	0.118	0.053
***p<0.05, **p<0.01**					

Table 5.2 shows that in trimester 1, dietary pattern 4, which was characterised by high intakes of eggs and fresh fruit, and low intakes of soft fruit juice, pulses and refined cereals, was moderately positively associated with rate of GWG in trimester 2 ($r=0.266$, $p<0.05$), which is shown in Figure 5.1. No other associations were observed between any other dietary pattern and any other GWG outcomes ($p>0.05$).

Table 5.2 Pearson correlations for Trimester 1 dietary patterns and GWG outcomes

	Pattern 1 score	Pattern 2 score	Pattern 3 score	Pattern 4 score	Pattern 5 score
Trimester 1 GWG, kg	-0.101	0.162	0.233	0.110	-0.030
Trimester 2 GWG, kg/week	-0.080	0.042	0.001	0.266*	0.195
Trimester 2 FM gain, kg/week (n=65)	-0.043	0.025	-0.049	0.093	0.113
Trimester 2 FFM gain, kg/week (n=65)	-0.036	0.015	0.072	0.196	0.076
***p<0.05, **p<0.01**					

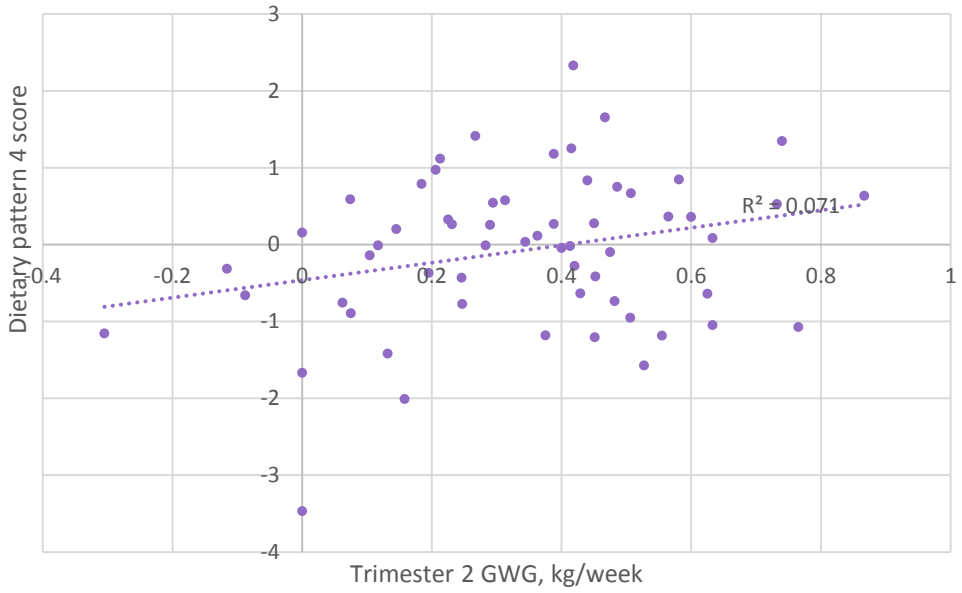


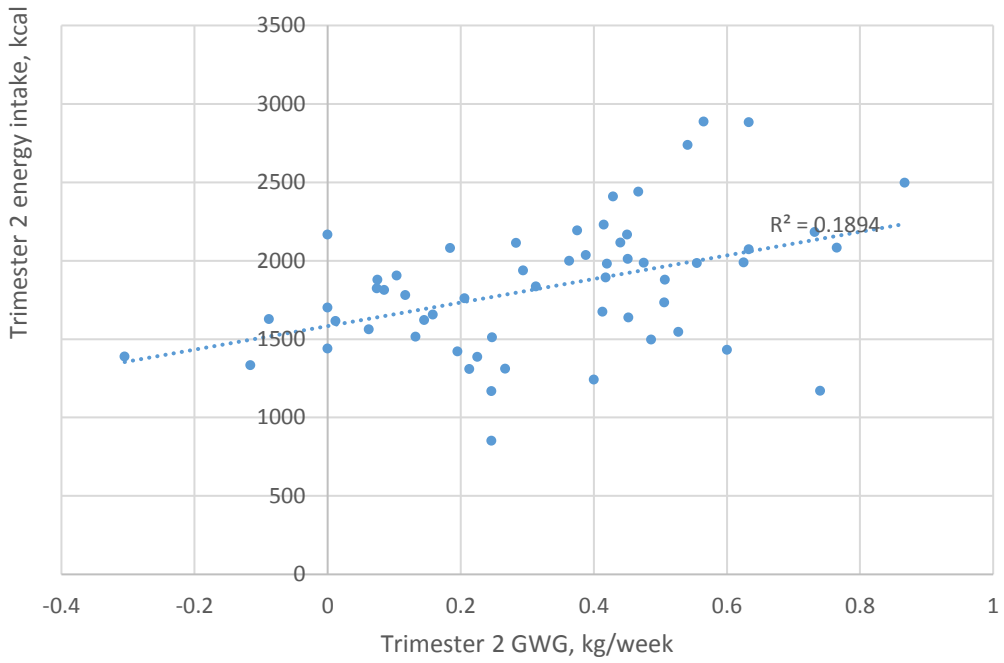
Figure 5.1 Correlations for trimester 1 dietary pattern scores and GWG, p<0.05

Table 5.3 shows that in trimester 2, a moderately positive relationship was observed between mean EI and rate of GWG (r=0.435) and rate of FM accrual (r=0.394) (all p<0.01), with no association observed between rate of FFM accrual and EI (p>0.05). These relationships are shown in Figure 5.2. No associations between any GWG

outcomes and the proportion of energy coming from any macronutrient were observed (p>0.05).

Table 5.3 Pearson correlations for Trimester 2 GWG and dietary intake, n=58

	Energy, kcal	% energy CHO	% energy sugar	% energy fat	% energy protein
Trimester 2 GWG, kg/week	0.435**	0.190	0.147	-0.160	-0.130
Trimester 2 FM gain, kg/week	0.394**	0.131	0.078	-0.093	-0.106
Trimester 2 FFM gain, kg/week	-0.052	0.037	0.065	-0.056	-0.001
***p<0.05, **p<0.01**					



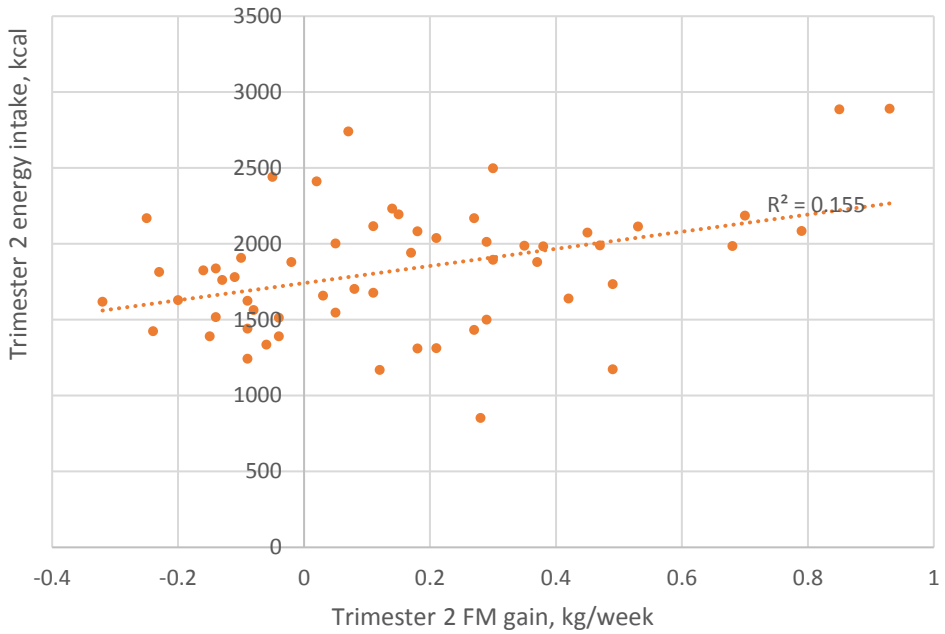
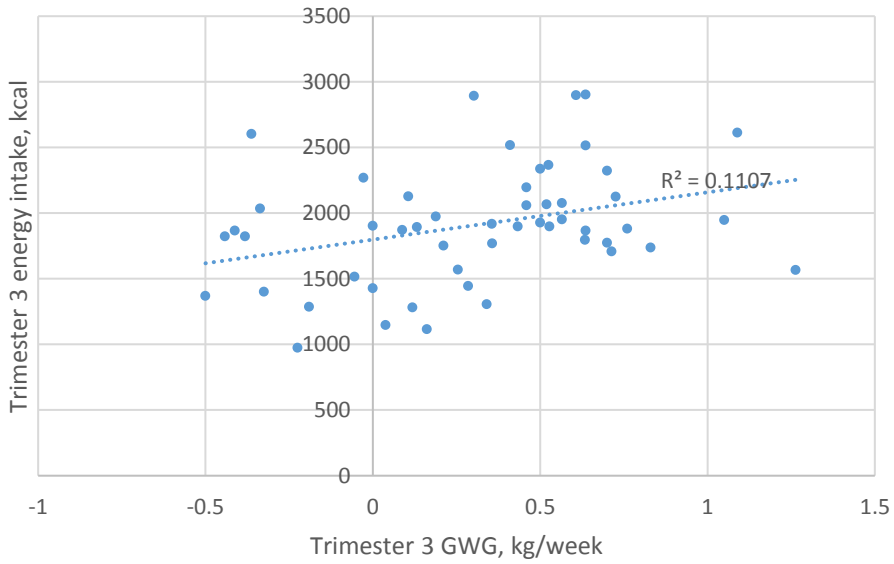


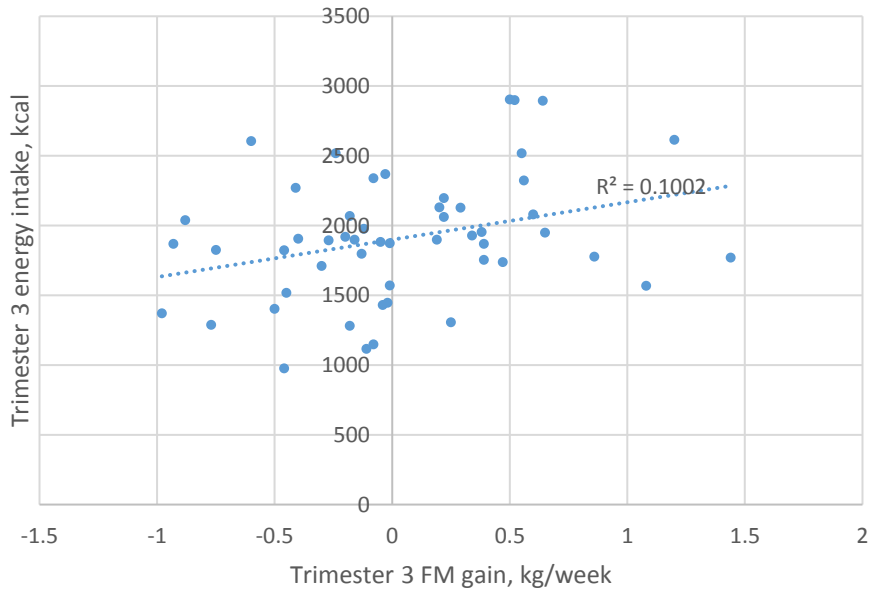
Figure 5.2 Trimester 2 correlations for changes in maternal body composition and maternal energy intake, p<0.05

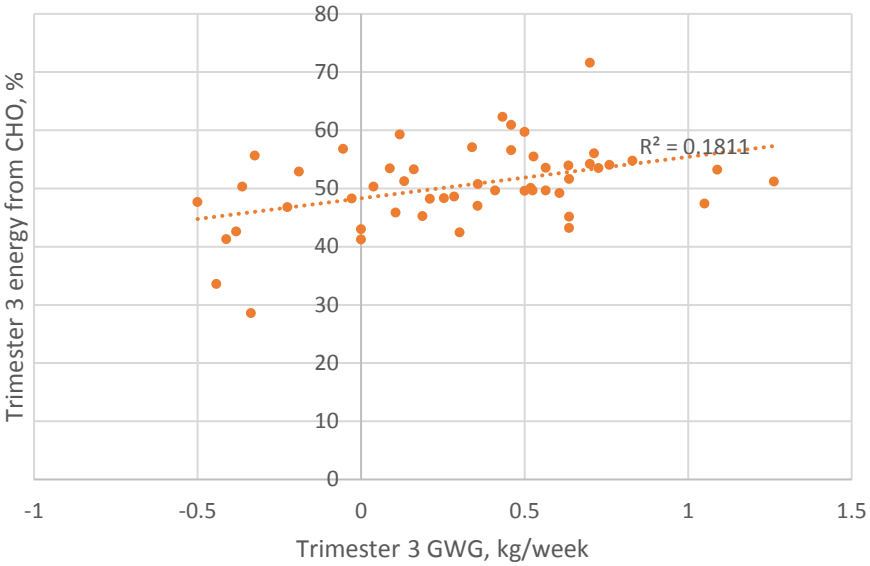
Table 5.4 shows that a moderate positive relationship was observed between trimester 3 GWG and mean EI (r=0.333, p<0.05), proportion of energy from CHO (r=0.426, p<0.01) and proportion of energy from sugar (r=0.348, p<0.05). There was also a negative association observed between proportion of energy from protein and GWG (r=-0.300, p<0.05). There was a moderate positive association between trimester 3 FM accrual and EI (r=0.317, p<0.05) with a negative association observed for the proportion of energy from protein (r=-0.274, p<0.05). These relationships are shown graphically in Figure 5.3. There was no relationship observed between trimester 3 FFM accrual and any dietary measure (p>0.05).

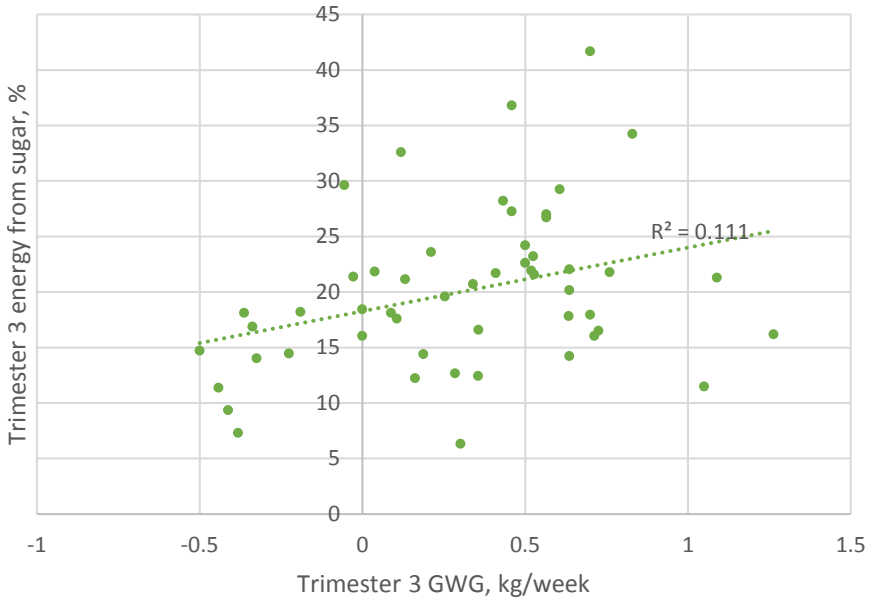
Table 5.4 Pearson correlations for Trimester 3 GWG and dietary intake, n=52

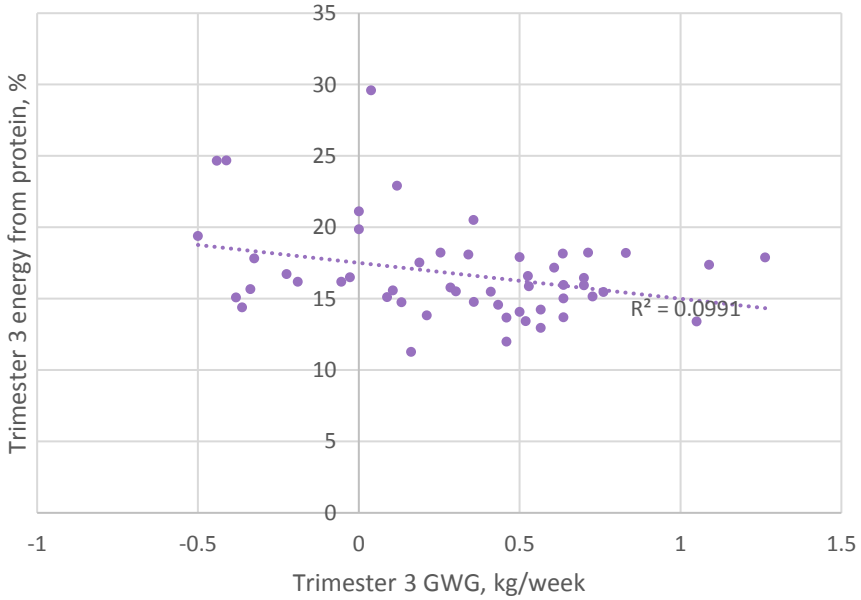
	Energy, kcal	% energy CHO	% energy sugar	% energy fat	% energy protein
Trimester 3 GWG, kg/week	0.333*	0.426**	0.348*	-0.266	-.300*
Trimester 3 FM gain, kg/week	0.317*	0.272	0.227	-0.127	-0.274*
Trimester 3 FFM gain, kg/week	-0.092	0.099	0.074	-0.134	0.068
***p<0.05, **p<0.01**					






Trimester 3 energy from CHO, %
80
70
60
50
40
30
20
10
0
-1
-0.5
0
0.5
1
1.5
Trimester 3 GWG, kg/week
R² = 0.1811


Trimester 3 energy from sugar, %
45
40
35
30
25
20
15
10
5
0
-1
-0.5
0
0.5
1
1.5
Trimester 3 GWG, kg/week
R² = 0.111


Trimester 3 energy from protein, %
35
30
25
20
15
10
5
0
-1
-0.5
0
0.5
1
1.5
Trimester 3 GWG, kg/week
R² = 0.0991

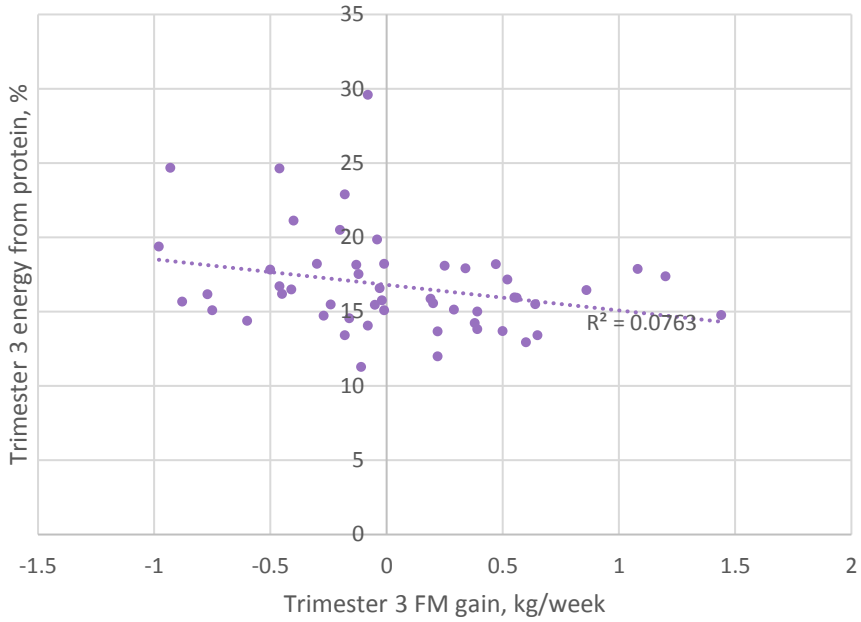


Figure 5.3 Trimester 3 correlations for changes in maternal body composition and maternal energy intake, p<0.05

5.1.1.1 Diet and Institute of Medicine gestational weight gain guidelines

Table 5.5 shows mean daily energy and macronutrient intakes for women by GWG category as classified by IOM guidelines in trimesters, one, two and three.

In trimester 1, women who gained within IOM GWG guidelines appeared to have a higher mean EI of 1943 ± 277 kcal compared to women gaining below (1636 ± 419 kcal) and above (1845 ± 511 kcal) the guidelines, although the model did not quite reach significance ($F(2,63) = 2.886$, $p=0.063$).

Table 5.5 Macronutrient intake by GWG category

Trimester 1 (n=66)	**Insufficient (n=31)**	**Adequate (n=13)**	**Excessive (n=22)**	**p**
Energy				
Energy (kcal)	1636 ± 419	1943 ± 277	1845 ± 511	0.063
CHO				
Energy from CHO (%)	54.3 ± 6.6	52.4 ± 7.9	52.7 ± 6.7	0.600
Energy from sugars (%)[a]	21.7 {19.4 -24.2}	21.2 {17.2 -26.0}	20.2 {17.5 -23.3}	0.714
Fat				
Energy fat (%)	22.3 ± 8.2	34.6 ± 5.2	35.4 ± 5.1	0.477
Energy saturated fat (%)	12.2 ± 2.6	12.5 ± 3.2	11.9 ± 2.5	0.845
Protein				
Energy from protein (%)[a]	15.3 ± 3.2	16.2 ± 3.2	15.1 ± 3.1	0.563
Trimester 2 (n=58)	**Insufficient (n=16)**	**Adequate (n=9)**	**Excessive (n=33)**	**p**
Energy				
Energy (kcal)	1677 ± 214	1422 ± 348	2014 ± 408	<0.005*
CHO				
Energy CHO (%)	49.3 ± 7.6	53.6 ± 6.4	52.2 ± 6.3	0.243
Energy sugars (%)	18.9 ± 6.8	23.6 ± 7.9	20.9 ± 7.2	0.328
Fat				
Energy fat (%)	36.1 ± 5.2	32.2 ± 5.0	34.4 ± 5.6	0.222
Energy saturated fat (%)	12.7 ± 3.1	12.8 ± 2.0	12.7 ± 2.9	0.981
Protein				
Energy protein (%)[a]	17.2 {15.7 -18.9}	17.2 {15.5 -19.1}	15.9 {14.8 -17.2}	0.341
Trimester 3 (n= 52)	**Insufficient (n=19)**	**Adequate (n=3)**	**Excessive (n=30)**	**p**
Energy				
Energy (kcal)	1670 ± 435	1765 ± 204	2076 ± 412	0.006*
CHO				
Energy CHO (%)	47.5 ± 7.8	47.3 ± 1.7	52.8 ± 5.9	0.023*
Energy sugars (%)	17.6 ± 6.2	19.2 ± 4.6	21.7 ± 7.6	0.142
Fat				
Energy fat (%)	37.0 ± 7.8	39.0 ± 2.3	34.5 ± 5.7	0.287
Energy saturated fat (%)[a]	14.4 {12.6 -16.4}	15.5 {8.0 – 25.4}	12.9 {11.6 -14.3}	0.239
Protein				
Energy protein (%)[a]	17.8 {15.9 -19.9}	16.4 {11.3 -23.8}	15.7 {15.0 -16.4}	0.052

Mean ± SD

[a]Mean calculated by back-transformation {CI}

In trimester 2, EI was different between GWG categories ($F(2,55)= 11.797$, $p<0.0005$). Tukey posthoc analysis revealed that mean EI in women who gained above the guidelines (2014 ± 408 kcal) was significantly higher than mean EI for women who gained within (1422 ± 348 kcal, $p<0.005$) and below the guidelines (1677 ± 214 kcal, $p=0.008$), but there were no differences between women who gained within and below the guidelines ($p=0.209$). Percentage energy was not significantly different between IOM category for any nutrient ($p>0.05$).

As in trimester 2, EI was different between GWG categories for trimester 3 ($F(2,49)=5.776$), $p=0.006$). Tukey posthoc analysis revealed that mean EI for women who gained in excess of the recommendations (2076 ± 412 kcal) was significantly higher than in women gaining below recommendations (1670 ± 435 kcal, $p=0.004$), but was not significantly different to those gaining within the recommendations (1765 ± 204 kcal, $p=0.437$). Only percentage energy from CHO was significantly different between IOM categories ($F(2,49)=4.097$, $p=0.023$). Tukey posthoc analysis revealed that percentage energy from CHO was significantly higher in women who gained above recommendations (52.8 ± 5.9 %) than in women who gained below recommendations (47.5 ± 7.8 %, $p=0.024$), while there was no difference between those who gained within and above the recommendations ($p=0.363$).

5.1.2 **Diet and gestational diabetes mellitus**

Table 5.6 shows trimester 1 macronutrient intake by GDM diagnosis. Percentage energy from sugar was significantly higher in women who went on to develop GDM (24.8, 95% CI 20.4, 30.1 %) than in women who did not develop GDM (20.2, 95% CI

18.7, 21.8 % ; p= 0.017). No other differences were observed between intakes of other nutrients and the two groups of women (p>0.05).

Table 5.6 Mean daily trimester 1 macronutrient intake by GDM diagnosis.

	+ve GDM diagnosis (n=17)	-ve GDM diagnosis (n=47)	p
Energy			
Energy (kcal)[a]	1796 {1588 – 2033}	1703 {1573-1844}	0.490
CHO			
Energy from CHO (%)	54.8 ± 8.0	53.1 ± 6.4	0.376
Energy from sugars (%)[a]	24.8 {20.4 – 30.1}	20.2 {18.7 –21.8}	0.017*
Fat			
Energy from fat (%)	33.0 ± 5.8	34.7 ± 4.2	0.208
Energy from saturated fat (%)	11.4 ± 3.5	12.3 ± 2.3	0.251
Protein			
Energy from protein (%)[a]	15.1 {13.5 – 16.7}	15.2 {14.4 – 16.1}	0.915

Mean ± SD, independent t test (2 tailed)
[a]Mean calculated by back-transformation {CI}, independent t test (2 tailed)
*p<0.05, **p<0.01

As shown previously in Table 4.5, the visit made to women at the end of second trimester was at median gestation of 28^{+4} and ranged from 27^{+1} – 29^{+6}. Diet diaries were generally completed for the four consecutive days following this visit, which meant that some women would have completed their OGTT and received a result, whereas others would not yet have taken their test and/or not received their result. Macronutrient intake in trimester 2 has therefore not been analysed by GDM diagnosis, as some women may have already changed their diet during the recording period in response to a GDM diagnosis.

Table 5.7 shows that there were no significant differences between those who developed GDM and those who did not for any of the dietary patterns in trimester 1.

Table 5.7 Trimester 1 dietary pattern scores and GDM diagnosis (n=64)

	+ve GDM (n=17)	-ve GDM (n=47)	p
Pattern 1 score	0.304 ± 0.953	-0.091 ± 1.022	0.171
Pattern 2 score[a]	0.036 {-0.348 – 0.518}	-0.257 {-0.505 – 0.036}	0.276
Pattern 3 score[b]	-0.430 (0.619)	0.069 (1.341)	0.072
Pattern 4 score	-0.207 ± 1.167	0.042 ± 0.940	0.383
Pattern 5 score	-0.097 ± 0.967	0.070 ± 1.00	0.556

Mean ± SD, independent t test (2 tailed)
[a]Mean calculated by back-transformation {CI}
[b]Median (IQR), Mann-Whitney U Test

5.1.3 **Diet and infant birth size**

In trimester 1, no significant relationships were observed between any dietary intakes or infant birth size characteristics (Table 5.8).

Table 5.8 Pearson correlations for Trimester 1 dietary intake and infant birth size outcomes

	N=64		N=53		
	Birth weight centile	**Birth weight z-score**	**Triceps SFT, mm**	**UFE, cm^2**	**UME, cm^2**
Energy, kcal	0.052	0.032	0.161	0.167	0.049
% energy CHO	0.108	0.095	-0.066	-0.065	0.091
% energy sugar	0.098	0.096	-0.041	-0.015	0.153
% energy fat	-0.091	-0.093	0.161	0.163	-0.105
% energy protein	-0.070	-0.034	-0.064	-0.076	-0.038

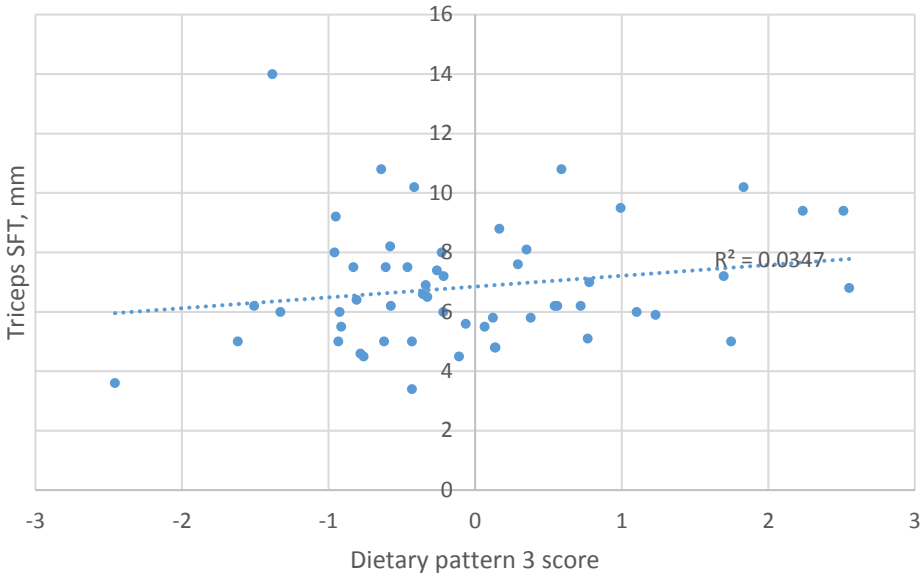
***p<0.05, **p<0.01**
UFE – upper arm area fat estimate
UME – upper arm area muscle estimate

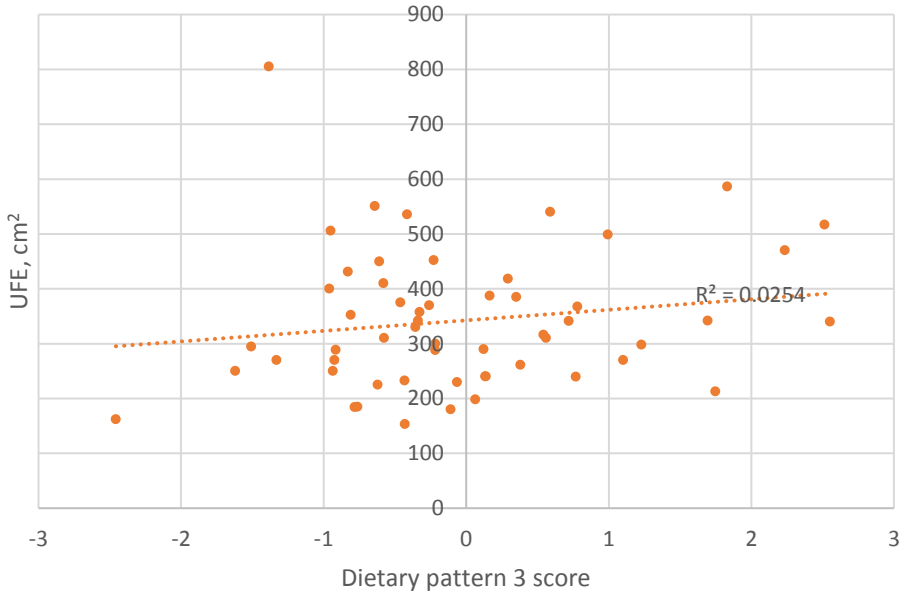
Table 5.9 shows there were no associations between any of the dietary patterns identified in trimester 1 and birth weight outcomes ($p>0.05$). Pattern 3, which was characterised by high intakes of white bread, butter, added sugar, baked potatoes, cakes and biscuits, and by low intakes of wholemeal bread, showed a moderate, positive relationship with infant triceps SFT ($r=0.316$) and infant UFE ($r=0.299$, all $p<0.05$). There was also a moderate positive relationship between pattern 5, which was characterised by high intakes of baked beans, pasta/noodles and chocolate and low intakes of coffee and infant UME ($r=0.313$, $p<0.05$). These relationships are shown graphically in Figure 5.4.

Table 5.9 Pearson correlations for Trimester 1 dietary patterns and infant birth size outcomes

	N=64 Birth weight centile	**Birth weight z-score**	**N=53 Triceps SFT, mm**	**UFE, cm^2**	**UME, cm^2**
Pattern 1 score	0.001	0.020	0.018	0.007	0.090
Pattern 2 score	-0.123	-0.130	-0.035	-0.058	-0.091
Pattern 3 score	0.213	0.182	0.316*	0.299*	-0.116
Pattern 4 score	-0.035	-0.011	-0.076	0.001	0.202
Pattern 5 score	0.159	0.151	-0.098	-0.032	0.312*

***p<0.05, **p<0.01**
UFE – upper arm area fat estimate
UME – upper arm area muscle estimate





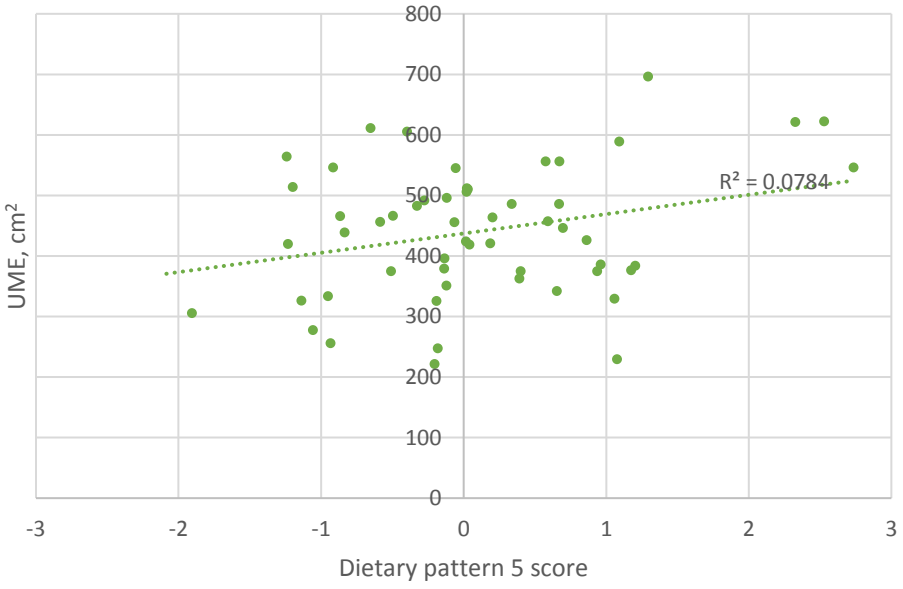


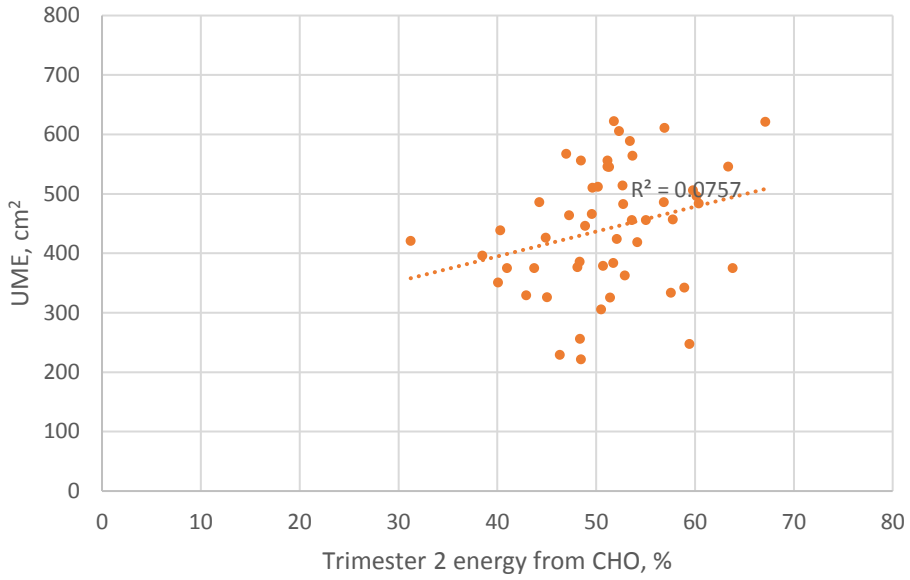
Figure 5.4 Correlations for trimester 1 dietary pattern scores and infant body composition, p<0.05

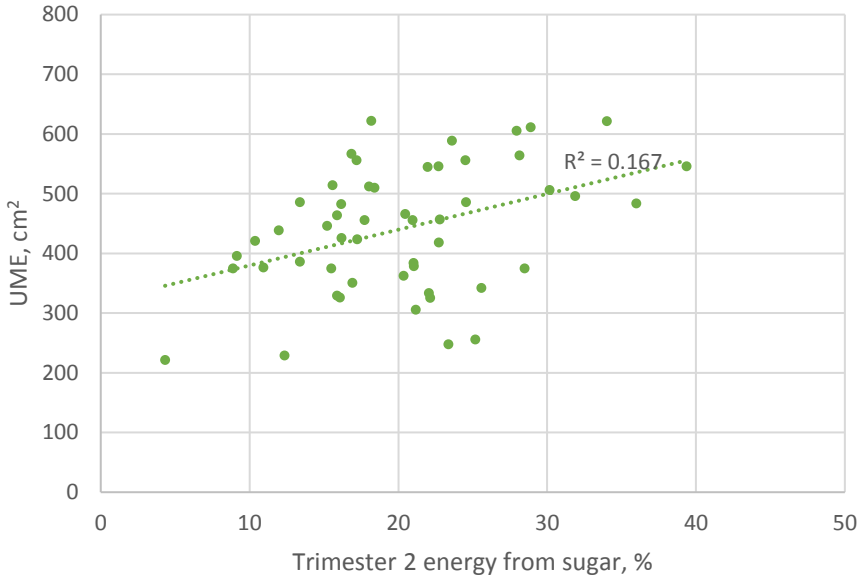
In trimester 2, only percentage energy from carbohydrate, sugar and fat were significantly related to infant UME (Table 5.10). There was a moderate positive relationship between percentage energy from carbohydrate (r=0.319, p<0.05) and sugar (r=0.419, p<0.01) and a moderate negative relationship between percentage energy from fat and infant UME (r=0.440, p<0.01; Figure 5.5). No other significant relationships were observed between dietary intakes and other infant birth size outcomes.

Table 5.10 Pearson correlations for Trimester 2 dietary intake and infant birth size outcomes

	N=54		**N=50**		
	Birth weight centile	**Birth weight z-score**	**Triceps SFT, mm**	**UFE, cm^2**	**UME, cm^2**
Energy, kcal	-0.066	-0.074	-0.026	0.000	0.067
% energy CHO	0.024	0.044	-0.028	0.053	0.319*
% energy sugar	0.046	0.073	-0.042	0.075	0.419**
% energy fat	-0.092	-0.122	0.042	-0.081	-0.440**
% energy protein	0.080	0.093	-0.002	0.038	0.090

***p<0.05, **p<0.01**
UFE – upper arm area fat estimate
UME – upper arm area muscle estimate





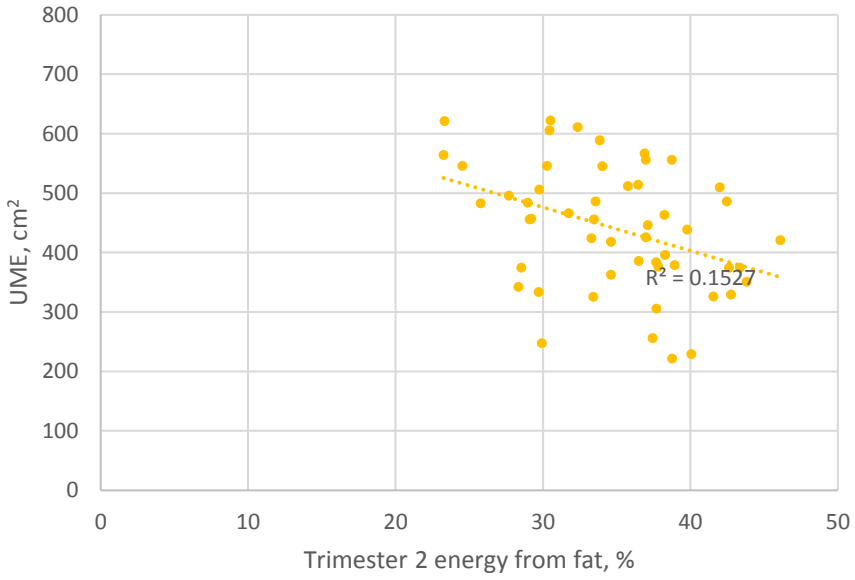


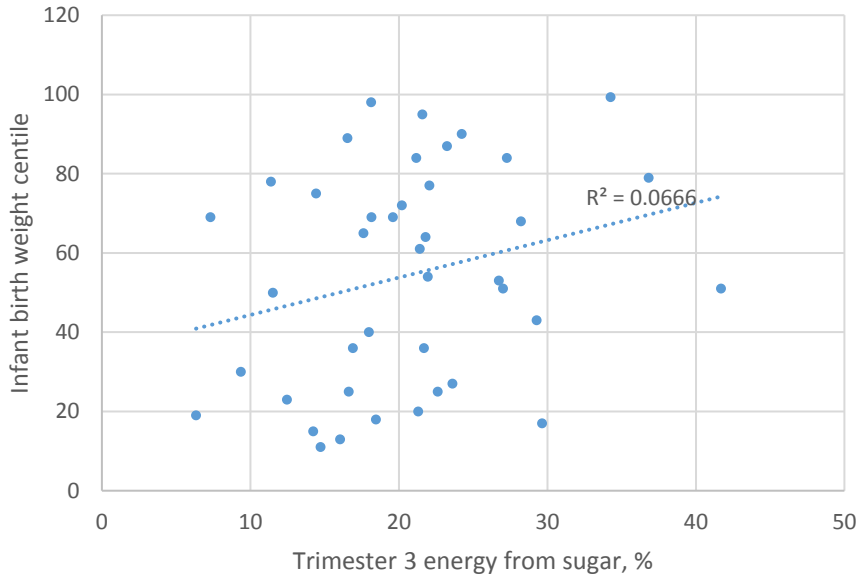
Figure 5.5 Correlations for trimester 2 dietary intakes and infant body composition, p<0.05

Similarly to trimester 2, a moderate positive relationship between percentage energy from sugar and infant UME was observed in trimester 3 (r=0.376, p<0.01), as well as a moderate inverse relationship between percentage energy from fat and infant UME (r=-0.292, p<0.05; Table 5.11). A moderate positive relationship was also observed between both infant birth weight centile and z-score and proportion of energy from sugar (r=0.289 and r=0.308, p<0.05; Figure 5.6). No other significant relationships were observed between dietary intakes and other infant birth size outcomes.

Table 5.11 Trimester 3 dietary intake and infant birth size outcomes

	N=52		N=50		
	Birth weight centile	**Birth weight z-score**	**Triceps SFT, mm**	**UFE, cm^2**	**UME, cm^2**
Energy, kcal	0.056	0.041	-0.072	-0.074	0.039
% energy CHO	0.192	0.211	0.139	0.188	0.225
% energy sugar	0.289*	0.308*	-0.036	0.066	0.376**
% energy fat	-0.160	-0.182	-0.101	-0.160	-0.292*
% energy protein	-0.072	-0.057	-0.092	-0.076	0.130

***p<0.05, **p<0.01**



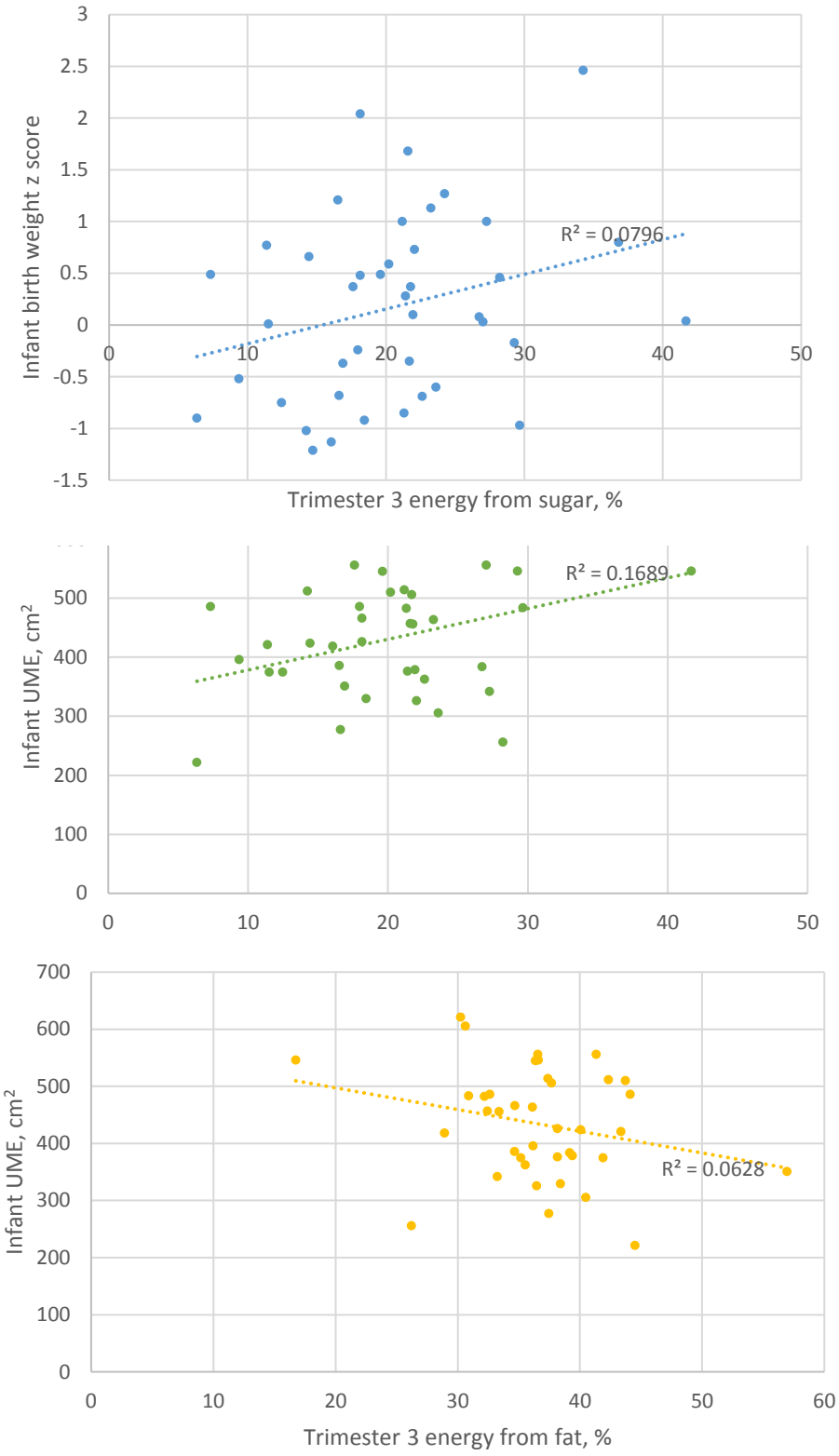


Figure 5.6 Correlations for trimester 3 dietary intakes and infant body composition, p<0.05

5.2 How does physical activity affect maternal and infant outcomes?

5.2.1 **Physical activity and gestational weight gain**

As shown in Table 5.12, no significant relationships were observed between any GWG outcomes at any point in pregnancy and physical activity measures (p>0.05).

Table 5.12 Pearson correlations for Trimester 1 GWG and physical activity, n=63

	Freedson cut points (% valid WT)			Step counts, mean steps/minute
	Sedentary (0-99 cpm)	Light (100-1951 cpm)	MVPA (≥1951 cpm)	
Trimester 1 (n=63)				
GWG, kg	-0.049	0.074	0.007	0.056
Trimester 2 (n=52)				
GWG, kg/week	-0.058	-0.032	0.152	0.147
FM gain, kg/week	-0.042	-0.115	0.243	0.122
FFM gain, kg/week	-0.014	0.127	-0.156	0.017
Trimester 3 (n=47)				
GWG, kg/week	-0.104	0.191	-0.086	0.105
FM gain, kg/week	-0.118	0.181	-0.050	0.127
FFM gain, kg/week	0.064	-0.057	-0.027	-0.078
***p<0.05, **p<0.01**				

5.2.1.1 Physical activity and Institute of Medicine gestational weight gain guidelines

Table 5.13 shows physical activity scoring data by GWG category for trimesters 1, 2 and 3. In trimester 1, only time spent in MVPA per day was significantly different between IOM = categories ($F(2,60) = 3.835$, $p=0.027$). Posthoc analysis revealed that women gaining within the GWG guidelines spent significantly more time in MVPA (243.1 ± 45.5 minutes/day) than those who gained below the guidelines (186.7 ± 76.7 minutes/day, p=0.048) and those who gained above the guidance (180.9 ± 69.8 minutes/day, p=0.031).

As in trimester 1, time spent in MVPA appears to change across GWG categories in trimester 2, although this does not quite reach significance for either the proportion of time spent in MVPA ($F(2, 49)=2.871$, $p=0.066$) nor the time in minutes spent in MVPA ($F(2.49)=2.770$, $p=0.072$).

In trimester 3, the time spent in LPA was significantly different between groups ($F(2,44)=4.367$, $p=0.015$) with posthoc analysis revealing that LPA was significantly higher amongst women gaining within the IOM guidelines (49.1 ± 11.2 %) than women gaining below the guidelines (35.8 ± 4.2%, $p=0.012$). However, this is perhaps not an appropriate test as only three women were classified as gaining within GWG guidelines in trimester 3.

Table 5.13 Physical activity scoring data by GWG category in trimesters 1, 2 and 3.

Trimester 1 (n=63)	**Insufficient (n=27)**	**Adequate (n=13)**	**Excessive (n=23)**	**p**
Freedson Cut Points (% of valid WT)				
Sedentary (0-99 cpm)	46.3 ± 12.0	46.2 ± 5.5	47.0 ± 9.3	0.966
Light (100-1951 cpm)	37.9 ± 6.6	35.6 ± 3.4	38.4 ± 6.2	0.401
MVPA (≥ 1951 cpm)	15.8 ± 8.2	18.1 ± 3.5	14.7 ± 6.3	0.344
Mean MVPA/day (min)	186.7 ± 76.7	243.1 ± 45.5	180.9 ± 69.8	0.027*
Step counts				
Mean counts/minute	9.5 ± 3.6	9.7 ± 1.9	9.3 ± 2.6	0.917
Trimester 2 (n=52)	**Insufficient (n=13)**	**Adequate (n=8)**	**Excessive (n=31)**	**p**
Freedson Cut Points (% of valid WT)				
Sedentary (0-99 cpm)	45.8 ± 7.6	46.0 ± 4.5	43.8 ± 10.1	0.706
Light (100-1951 cpm)	42.0 ± 6.8	40.0 ± 6.0	40.4 ± 7.8	0.758
MVPA (≥ 1951 cpm)	12.2 ± 5.8	13.9 ± 4.2	15.8 ± 4.4	0.066
Mean MVPA/day (min)	146.7 ± 77.7	185.7 ± 67.8	194.8 ± 52.9	0.072
Step counts				
Mean counts/minute	8.5 ± 1.5	8.2 ± 1.4	9.3 ± 2.3	0.237
Trimester 3 (n= 52)	**Insufficient (n=15)**	**Adequate (n=3)**	**Excessive (n=29)**	**p**
Freedson Cut Points (% of valid WT)				
Sedentary (0-99 cpm)	47.4 ± 6.7	38.8 ± 11.6	46.3 ± 10.0	0.338
Light (100-1951 cpm)	35.8 ± 4.2	49.1 ± 11.2	39.2 ± 7.7	0.015
MVPA (≥ 1951 cpm)	16.8 ± 5.6	12.1 ± 5.3	14.6 ± 5.8	0.314
Mean MVPA/day (min)	210.6 ± 69.1	125.0 ± 68.8	180.4 ± 71.4	0.131
Step counts				
Mean counts/minute	8.8 ± 2.0	8.6 ± 1.7	8.5 ± 2.2	0.946

Mean ± SD, one-way ANOVA

5.2.2 **Physical activity and infant birth size**

There were no significant relationships observed between physical activity outcomes in any trimester and infant birth size outcomes (p>0.05) as shown in Table 5.14.

Table 5.14 Trimester 1, 2 and 3 physical activity and infant birth size outcomes.

	Birth weight centile	**Birth weight z-score**	**Triceps SFT, mm**	**UFE, cm^2**	**UME, cm^2**
Trimester 1 (n=59)					
Freedson cut points (% valid WT)					
Sedentary (0-99 cpm)	-0.043	-0.026	-0.109	-0.138	-0.046
Light (100 – 1951 cpm)	-0.075	-0.056	0.027	0.054	0.061
MVPA (≥ 1951 cpm)	0.129	0.087	0.132	0.151	0.015
Step counts, steps/minute	0.03	0.001	0.035	0.078	0.109
Trimester 2 (n=48)					
Freedson cut points (% valid WT)					
Sedentary (0-99 cpm)	0.129	0.152	0.032	0.088	0.148
Light (100 – 1951 cpm)	-0.150	-0.172	0.034	-0.010	-0.138
MVPA (≥ 1951 cpm)	0.005	-0.003	-0.110	-0.141	-0.045
Step counts, steps/minute	-0.121	-0.125	-0.122	-0.141	0.007
Trimester 3 (n=47)					
Freedson cut points (% valid WT)					
Sedentary (0-99 cpm)	-0.068	-0.101	-0.055	-0.057	-0.056
Light (100 – 1951 cpm)	0.120	0.169	0.025	0.033	0.094
MVPA (≥ 1951 cpm)	-0.049	-0.062	0.057	0.049	-0.040
Step counts, steps/minute	-0.051	-0.032	0.019	0.022	0.004

*p<0.05, **p<0.01
UFE – upper arm area fat estimate
UME – upper arm area muscle estimate
NB for infant body composition n=47, 45 and 44 in trimesters 1, 2 and 3, respectively.

5.3 Does the timing and composition of GWG affect infant birth weight and adiposity?

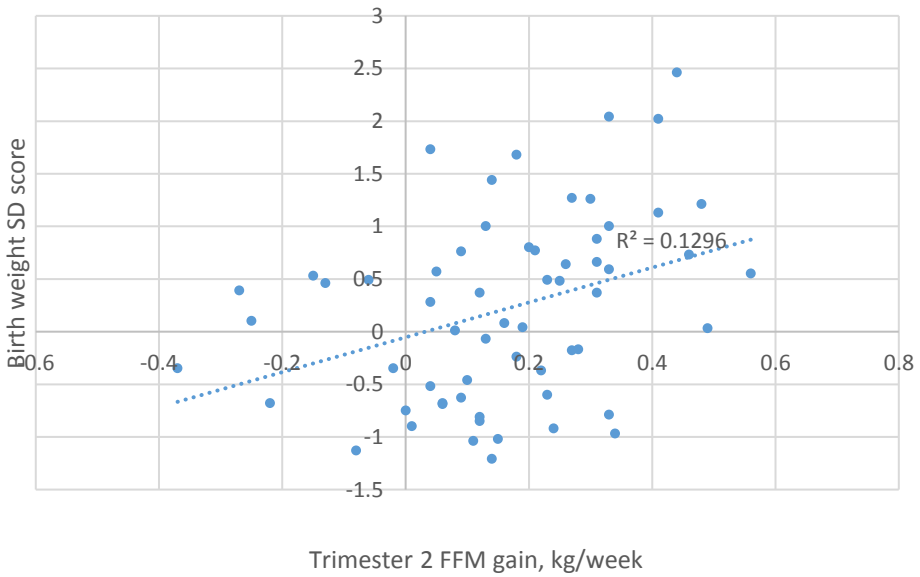
There were no significant relationships observed between total or trimester-specific GWG and infant birth weight or body composition measurements ($p>0.05$) as shown in Table 5.15.

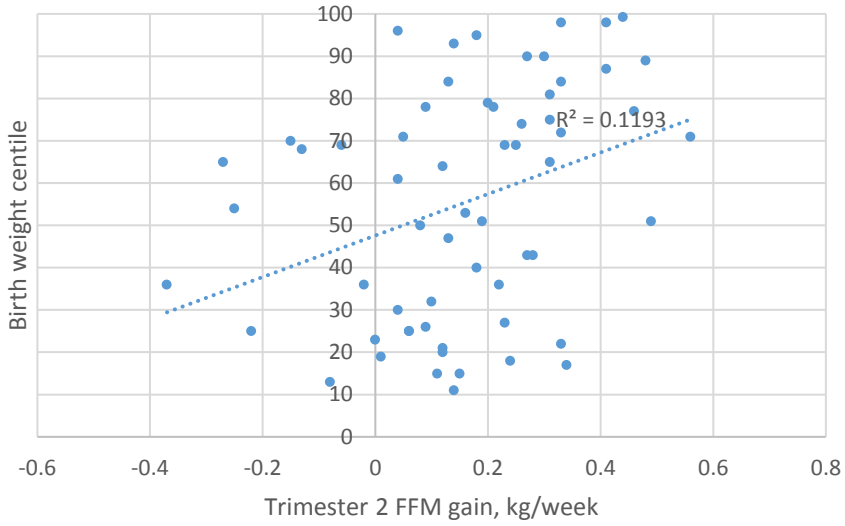
Table 5.15 Pearson correlations for changes in maternal body composition and infant birth size outcomes.

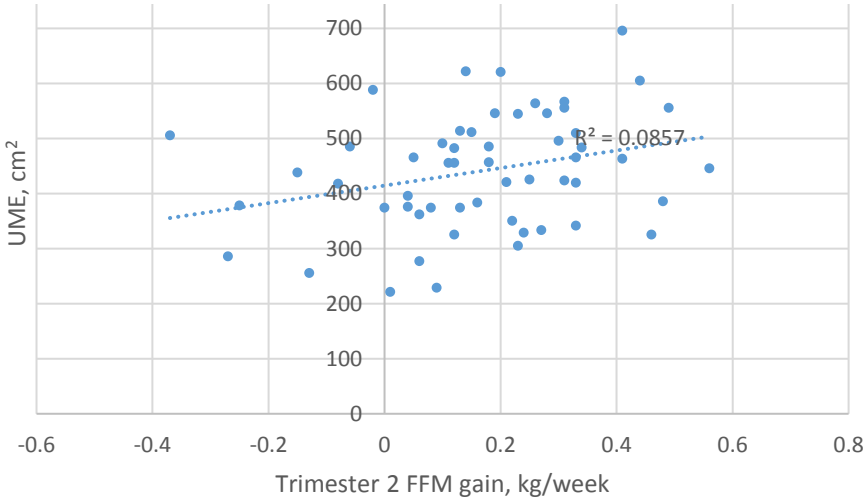
	Birth weight outcomes		**Infant body composition**		
	Birth weight centile	**Z-score**	**Infant triceps SFT, mm**	**UFE, cm^2**	**UME, cm^2**
Total (n=56)					
GWG, kg/week	0.105	0.124	0.028	0.094	0.231
FM gain, kg/week	-0.134	-0.121	0.30	0.039	.025
FFM gain, kg/week	0.460**	0.468**	-0.007	0.092	0.357**
Trimester 2 (n=61)					
GWG, kg/week	0.092	0.097	0.137	0.206	0.180
FM gain, kg/week	-0.155	-0.161	0.086	0.074	-0.048
FFM gain, kg/week	0.346**	0.360**	0.042	0.144	0.291*
Trimester 3 (n=56)					
GWG, kg/week	0.068	0.104	-0.121	-0.070	0.248
FM gain, kg/week	-0.059	-0.024	-0.040	-0.007	0.106
FFM gain kg/week	0.182	0.169	-0.085	-0.072	0.140

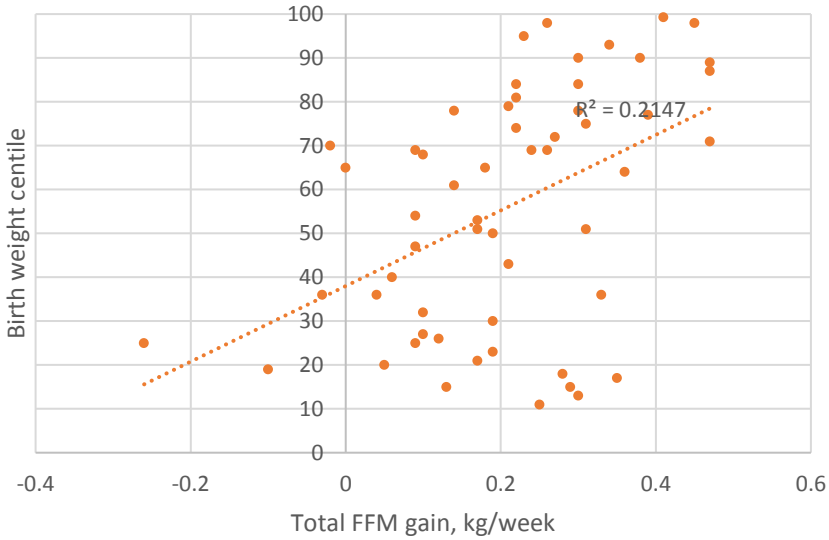
NB. For infant body composition outcomes n=53, 56 and 53 for total, trimester 2 and trimester 3 GWG, respectively. *p<0.05, **p<0.01
SFT – skinfold thickness
UFE – upper arm area fat estimate
UME – upper arm area muscle estimate

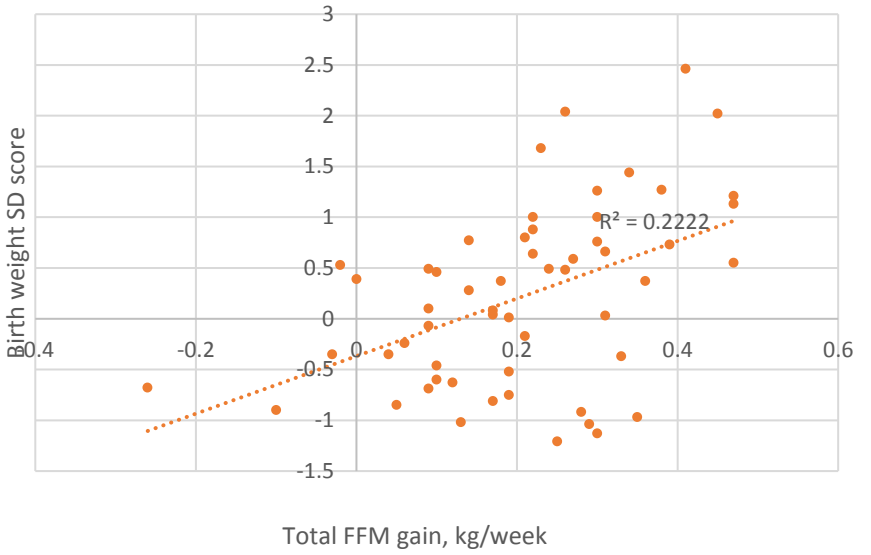
There was a moderate positive correlation between changes in FFM over total pregnancy and birth weight centile (r=0.460) and birth weight z-score (r=0.468) that were both statistically significant (all p<0.01). There was also a significant, moderate positive correlation between change in FFM during trimesters 2 and birth weight centile (r=0.346) and birth weight z-score (r=0.360) (all p<0.01). There was no significant relationship observed between change in FM and birth weight outcomes at any time point, nor for the change in FFM during trimester 3 (all p>0.05). There was a statistically significant moderate positive correlation between changes in FFM and infant UME over total pregnancy (r=0.357, p<0.01) and during trimester 2 (r=0.291, p<0.05). In contrast, there was no significant relationship observed between change in FM and infant body composition measurements at any time point (p>0.05) nor between changes in FFM and infant triceps SFT or UFE at any time point (p>0.05). Figure 5.7 shows scatter plots of the variables for which a significant relationship was observed.




Birth weight centile
Trimester 2 FFM gain, kg/week
R² = 0.1193
100
90
80
70
60
50
40
30
20
10
0
-0.6
-0.4
-0.2
0
0.2
0.4
0.6
0.8


UME, cm²
Trimester 2 FFM gain, kg/week
R² = 0.0857
700
600
500
400
300
200
100
0
-0.6
-0.4
-0.2
0
0.2
0.4
0.6
0.8


Birth weight centile
Total FFM gain, kg/week
R² = 0.2147
100
90
80
70
60
50
40
30
20
10
0
-0.4
-0.2
0
0.2
0.4
0.6



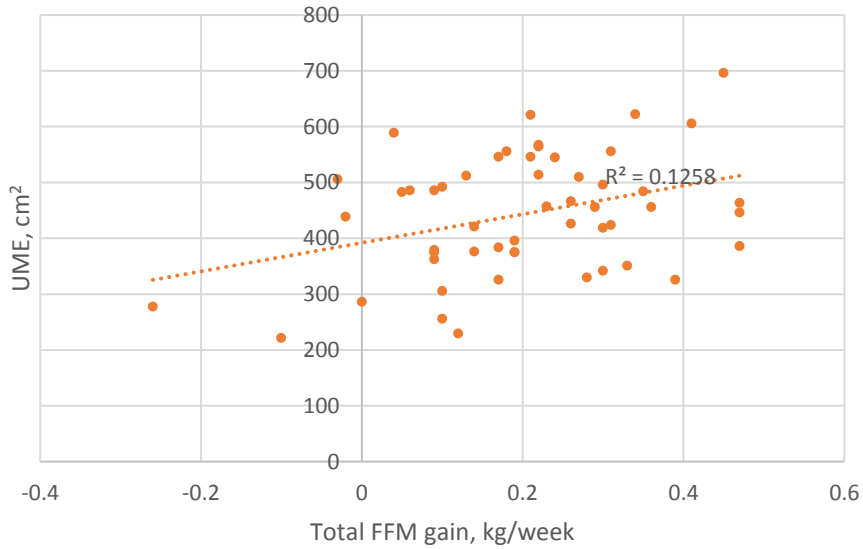


Figure 5.7 Correlations for changes in maternal body composition and infant birth size outcomes.

5.3.1 Infant birth size according to Institute of Medicine gestational weight gain guidelines

Table 5.16 shows infant birth weight data obtained from hospital notes, and table 5.17 shows infant anthropometrics obtained by the researcher during a home visit, by GWG category for trimesters 1, 2, 3 and total GWG. Category of GWG did not appear to

influence infant anthropometric outcomes, in any trimester nor across pregnancy, with no significant differences detected between groups (p>0.05).

Table 5.16 Infant birth weight by IOM GWG category in trimesters 1, 2 and 3.

Trimester 1 (n=71)	**Insufficient (n=34)**	**Adequate (n=13)**	**Excessive (n=24)**	**p**
Birth weight				
Birth weight centile	55.9 ± 27.4	58.5 ± 27.5	52.8 ± 26.0	0.818
Birth weight z-score	0.22 ± 0.89	0.33 ± 0.92	0.10 ± 0.79	0.710
Trimester 2 (n=61)	**Insufficient (n=17)**	**Adequate (n=8)**	**Excessive (n=36)**	**p**
Birth weight				
Birth weight centile[a]	69.0 (56.5)	57.0 (72.5)	52.0 (40.0)	0.746
Birth weight z-score	0.03 ± 0.87	0.49 ± 1.31	0.24 ± 0.79	0.483
Trimester 3 (n=56)	**Insufficient (n=22)**	**Adequate (n=3)**	**Excessive (n=31)**	**p**
Birth weight				
Birth weight centile	54.7 ± 27.8	57.0 ± 26.2	56.5 ± 27.9	0.969
Birth weight z-score	0.15 ± 0.86	0.18 ± 0.68	0.27 ± 0.93	0.892
Total (n=56)	**Insufficient (n=16)**	**Adequate (n=8)**	**Excessive (n=32)**	**p**
Birth weight				
Birth weight centile[a]	67.0 (49.8)	38.5 (68.5)	57.5 (39.0)	0.620
Birth weight z-score	0.00 ± 0.79	0.16 ± 1.19	0.34 ± 0.85	0.455

Mean ± SD, one way ANOVA
[a]Median (IQR), Kruskall-Wallis

Table 5.17 Infant anthropometrics by IOM GWG category in trimesters 1, 2 and 3.

Trimester 1	**Insufficient (n=24)**	**Adequate (n=12)**	**Excessive (n=20)**	**p**
Crown-heel length (n=56)				
Length centile	46.4 ± 25.9	50.0 ± 33.3	47.7 ± 30.9	0.917
Length z-score	-0.13 ± 0.82	-0.01 ± 1.15	-0.13 ± 0.96	0.922
Body composition (n=57)				
Triceps SFT (mm)	6.7 ± 2.3	7.5 ± 2.2	6.8 ± 1.6	0.503
UFE (cm^2)	332.4 ± 142.7	373.8 ± 131.3	336.6 ± 97.0	0.624
UME (cm^2)	447.2 ± 116.8	404.2 ± 82.0	447.0 ± 109.4	0.477
Trimester 2	**Insufficient (n=16)**	**Adequate (n=8)**	**Excessive (n=32)**	
Crown-heel length (n=56)				
Length centile	48.4 ± 26.8	39.4 ± 31.1	48.1 ± 30.1	0.734
Length z-score	-0.05 ± 0.82	-0.42 ± 1.16	-0.05 ± 0.94	0.602
Body composition (n=57)				
Triceps SFT (mm)[b]	6.8 {5.9-7.9}	6.4 {5.2-8.0}	6.5 {5.9-7.3}	0.847
UFE (cm^2)[b]	325.5 {265.7-398.8}	309.5 {228.9-418.6}	325.2 {289.0-366.1}	0.934
UME (cm^2)	410.1 ± 106.9	428.6 ± 96.8	452.6 ± 109.9	0.433
Trimester 3	**Insufficient (n=21)**	**Adequate (n=3)**	**Excessive (n=29)**	
Crown-heel length (n=56)				
Length centile	42.0 ± 29.9	46.0 ± 7.8	51.8 ± 30.0	0.507
Length z-score	-0.24 ± 0.97	-0.10 ± 0.20	0.03 ± 0.97	0.599
Body composition (n=57)				
Triceps SFT (mm)[b]	6.5 {5.8 – 7.2}	6.4 {4.4 – 9.4}	6.71 {6.0– 7.6}	0.898
UFE (cm^2)	326.6 ± 100.3	314.0 ± 95.7	358.7 ± 143.8	0.625
UME (cm^2)	427.0 ± 93.9	424.7 ± 119.7	449.6 ± 119.6	0.755
Total	**Insufficient (n=15)**	**Adequate (n=8)**	**Excessive (n=30)**	
Crown-heel length (n=56)				
Length centile	43.0 ± 25.2	43.3 ± 34.6	51.0 ± 30.1	0.629
Length z-score	-0.20 ± 0.77	-0.21 ± 1.15	0.01 ± 0.98	0.718
Body composition (n=57)				
Triceps SFT (mm)	6.5 ± 1.3	7.5 ± 3.1	6.9 ± 2.0	0.542
UFE (cm^2)	314.7 ± 81.6	376.7 ± 215.7	349.2 ± 115.2	0.467
UME (cm^2)	416.9 ± 102.5	387.2 ± 78.1	463.0 ± 114.5	0.141

Mean ± SD, one way ANOVA

[b]Mean calculated by back-transformation {CI}, one way ANOVA

5.4 Discussion

To the best of the author's knowledge, this is the first study that has examined the effect of diet and physical activity on trimester-specific GWG as rate of GWG, FM accrual and FFM accrual, and their subsequent effect on infant birth weight and body composition. In the following sections, the results will be discussed in respect to each of the three main research questions.

5.4.1 How does diet affect maternal and infant outcomes?

5.4.1.1 Diet and gestational weight gain

No relationship was observed in the present study between dietary intakes and GWG in trimester 1. This is unsurprising, as many women suffered from pregnancy sickness, which influenced their eating habits, and GWG is less reliable in this trimester than others as it was based on the difference between booking weight, recorded by the participant's midwife, at varying stages of gestation, and the weight measured by the researcher at study visit 1. In trimester 2, there was a significant positive association observed between EI and rate of GWG with no associations observed for any macronutrients and GWG. Trimester 3 GWG was positively associated with EI, energy from carbohydrate and energy from sugar, and inversely associated with energy from protein. The positive association observed between both carbohydrate and sugar intakes and rate of GWG is difficult to explain, as it is just an observation. It is difficult to know whether increased energy coming from CHO or sugar in the third trimester could be driving foetal growth, and thus resulting in increased GWG, or whether increased foetal growth, and thus GWG, is increasing the appetite of women, and thus

leading them to consume more foods high in CHO or sugars. The presence of GDM could also confound this association, and in a larger study, this could be accounted for. Somewhat similarly, an Icelandic cohort study observed a significant and positive association between EI in late, but not early pregnancy and GWG (Olafsdottir *et al.*, 2006). Our findings also agree to some extent with those from a German prospective cohort study where a positive relationship was observed between total GWG and EI, and sugar intake adjusted for total energy intake (Diemert *et al.*, 2016). However, the authors did not specify the time-point at which dietary information was collected for these analyses, and unlike the present study, relied on a single measure of GWG over total pregnancy and included women with all BMIs. Energy, protein and lipids of animal origin at the end of the second trimester were positively associated, and carbohydrates inversely associated with GWG up to the same time-point in a US cohort study, which was once again, based on total, rather than rate of GWG and included women of all weights (Lagiou *et al.*, 2004).

With the exception of energy, which is found to consistently correlate with GWG, there is no consistent evidence from the current work, nor from the literature to suggest optimal macronutrient composition of the maternal diet to promote optimal GWG, which is consistent with findings from a recent systematic review (Tielemans *et al.*, 2016). The authors reported large heterogeneity between studies, which prevented them from conducting a meta-analysis, and also suggested that the effect of macronutrients on GWG may depend on their interaction with other foods and macronutrients and that future studies should be adjusted accordingly.

5.4.1.1.1 Diet and Institute of Medicine gestational weight gain guidelines

Data was also examined for differences in dietary intakes between women gaining below, within and in excess of IOM rate of GWG guidelines. No differences were observed between groups in trimester 1, and in trimesters 2 and 3, EIs were significantly higher amongst women gaining in excess of guidelines compared with women gaining below (trimesters 2 and 3) and within (trimester 2) guidelines. In trimester 3, percentage energy from carbohydrate was also significantly higher for women gaining in excess of guidelines than for women gaining below guidelines. It should be noted that few women gained within IOM guidelines in trimesters 2 and 3 (n= 9 and n=3, respectively) and therefore results should be interpreted with caution, as the study was not powered to detect differences between IOM groups.

Similar findings were observed by Olafsdottir et al (2006) with EI increasing across GWG categories based on Icelandic guidelines amongst overweight women. In contrast to the present study, women gaining in excess of guidelines consumed a significantly lower proportion of energy from carbohydrate than women gaining below guidelines, and significantly greater proportion of energy from fat. Total EI was also associated with increased odds of excessive GWG amongst women participating in Project Viva in the US, and when the effects of substituting 5% energy from carbohydrate with other macronutrients was examined, increased odds of excessive GWG were observed for protein, saturated, polyunsaturated and trans fatty acids, and reduced odds for monounsaturated fatty acids (Stuebe, Oken and Gillman, 2009). These findings were based on the previous IOM GWG guidelines (Institute of Medicine, 1990), so

comparison with studies based on the present guidelines is limited, although recent studies examining the relationship between maternal diet and adherence to the most recent IOM guidelines are scarce, especially amongst women with obesity.

5.4.1.2 Diet and maternal body composition

With regards to changes in maternal body composition in the present study, rate of FM accrual was positively associated with EI in both trimesters 2 and 3, and in trimester 3 only, positively associated with energy from CHO and sugar, and inversely associated with energy from protein. Rate of FFM accrual was not related to dietary intake in either trimester. Few studies have examined the impact of maternal diet throughout pregnancy on maternal body composition. The STORK study set in Norway, showed that women in the highest quartile of EI at 30-32 weeks gestation had significantly greater increase in their sum of SFT between 14-16 weeks and 36-38 weeks gestation than women in the lowest quartile of EI after adjustment for maternal age (Mugaas, 2007). These findings are comparable with those in the present study, and suggest that EI is positively associated with maternal subcutaneous FM changes. However, both the present study and STORK study relied on measures of subcutaneous fat in relatively small and homogenous groups of women. As other studies examining the relationship between nutrient intakes and maternal body composition could not be identified, this highlights a gap in the literature and further research is required to examine the relationship between nutrient intakes and maternal FM and FFM changes throughout pregnancy.

5.4.1.3 Diet and infant birth size

In the present study, no relationships were observed between trimester 1 energy or macronutrient intakes and any infant birth size characteristics. In trimester 2, there were no associations observed between dietary intakes and birth weight, but the proportion of energy from carbohydrate and sugar were significantly and positively associated with infant UME, while the proportion of energy from fat was inversely associated with infant UME. The same observations persisted for trimester 3 macronutrient intakes and infant UME, although the relationship with energy from carbohydrate no longer reached significance. As well as being positively associated with infant UME, the proportion of energy from sugar was also positively associated with infant birth weight centile and z score in the third trimester. These findings in the third trimester could possibly be linked to the positive associations between the proportion of energy from CHO and sugar and rate of GWG in the third trimester. If, as previously discussed, GWG in the third trimester can be explained by increased growth of the foetus, with CHO and sugar providing the foetus with glucose as a substrate for growth. However, the association between rate of third trimester GWG and infant UME did not quite reach significance and a future study, with a larger sample size, may be able to explore these potential associations with greater power.

In contrast, no associations were observed between macronutrient intakes and birth weight or infant FFM in the Healthy Start Study, but in multivariate regression, energy from saturated fat was positively associated, and energy from sugar inversely associated with infant FM (Crume *et al.*, 2016). However, when the model was

adjusted for maternal BMI, the relationships were no longer significant, suggesting that maternal obesity is an important confounder in the relationship between maternal dietary intake and infant body composition. A UK prospective observational study observed an inverse relationship between EI in early pregnancy (median gestation 15.3 weeks) and infant birth weight, which appeared to be mediated by an inverse association between carbohydrate intake in early pregnancy and birth weight, with the influence of carbohydrates stronger for sugars than for starch (Godfrey *et al.*, 1996). No independent relationships between energy nor macronutrients in late pregnancy (median gestation 32.7 weeks) and birth weight were observed, however, when early pregnancy carbohydrate was accounted for, late pregnancy protein intake was inversely associated with birth weight, with the influence of protein strongest for meat, rather than dairy or cereal protein.

Secondary analyses performed on data from the TOP study in Denmark examined the relationship between carbohydrate intake and infant body composition and observed that late (36-37 weeks), but not early (11-14 weeks) intake of carbohydrate was significantly associated with infant FM assessed by DEXA, but not birth weight nor FFM (Renault *et al.*, 2015). The Danish National Birth Cohort showed a positive relationship between maternal glycaemic load (GL) at week 25 and infant birth weight amongst all women in the cohort, but when examined by BMI category, the relationship only remained significant amongst normal and overweight women (Knudsen *et al.*, 2013), while infant body composition was not examined. Finally, the ROLO study successfully reduced the GI of the diet amongst women in the intervention group in their study

amongst women in Ireland, compared with controls, although no differences in birth weight were observed between groups (Walsh *et al.*, 2012). Subsequent analysis revealed infants born to women in the intervention group had significantly lower thigh circumference than infants born to control mothers, but these were the only anthropometric differences observed between groups, with no differences observed for other circumferences nor skinfold measurements between groups (Donnelly *et al.*, 2014).

Energy and carbohydrate intake appear to consistently influence infant birth size, however, the direction of these relationships is not clear. Some studies, including the present study, observed positive associations between energy and/or carbohydrate intakes and birth weight or size (Knudsen *et al.*, 2013; Renault *et al.*, 2015), and others reported an inverse relationship (Godfrey *et al.*, 1996; Crume *et al.*, 2016). Variations in the methods used to assess maternal diet with respect to carbohydrates could explain these differences with some studies examining total carbohydrate and others splitting carbohydrates into starches and sugar, with some studies reporting intakes in g/day, and others a percentage contribution to energy. Other studies reported the GI or GL of maternal diet. Therefore, it is difficult to make comparisons between studies, as it is possible that associations between maternal carbohydrate intakes and infant birth size are being influenced by GI or GL, or vice versa.

5.4.1.4 Dietary patterns

As previously described, five dietary patterns were derived from first trimester diet diaries and the relationship between these patterns and GWG and infant birth size was

explored. Adherence to pattern 3, which was characterised by high intakes of white bread, butter, added sugar, baked potatoes, cakes and biscuits ,was positively associated with infant triceps skinfold and UFE in the present study. In contrast, a similar pattern described in a Japanese study was associated with increased risk of SGA (Okubo *et al.*, 2012). Pattern 4, which was characterised by high intakes of eggs and fruit, was associated with rate of GWG during trimester 2 in the present study, in contrast to other studies, which generally observed a positive association between 'processed' patterns and excessive GWG (Uusitalo *et al.*, 2009; Tielemans *et al.*, 2015). The present study is the first study, to our knowledge, that has examined the relationship between the composition of GWG and dietary patterns, for which no associations were observed. Nonetheless, the sample size in the present study was underpowered, and given the associations observed between total GWG and dietary patterns, the association between dietary patterns and the composition of GWG should be further explored in a larger sample of women. No differences between dietary pattern scores were observed between women who developed GDM and those who did not. This is in contrast to observations of reduced risk of GDM with higher 'prudent' or 'healthy' dietary pattern scores (Zhang *et al.*, 2006; Tryggvadottir *et al.*, 2016), and increased risk for 'processed' patterns (Zhang *et al.*, 2006; Flynn *et al.*, 2016), but as the present study was underpowered to detect differences for GDM, our findings should be interpreted with caution.

5.4.2 **How does physical activity affect maternal and infant outcomes?**

5.4.2.1 Physical activity and gestational weight gain

No associations were observed between GWG and physical activity scoring measures in any trimester of pregnancy amongst participants in the present study. These findings are in keeping with those observed by Ruifrok et al. (2014) who did not observe any significant interactions between objectively measured sedentary or physical activity and GWG nor rate of GWG. Montpetit et al. (2012) observed an inverse association between steps/day and total GWG although no relationship was observed between MET hours/week, and GWG amongst 59 Canadian pregnant women. However, in this study, physical activity was estimated from the Pregnancy and Physical Activity Questionnaire (PPAQ), which although validated in a small sample of pregnant women (Chasan-Taber *et al.*, 2004), subjective physical activity questionnaires have been shown to perform poorly amongst pregnant women , and objective methods of assessment are preferred as a gold standard for accuracy (Harrison *et al.*, 2011).

With regards to IOM GWG guidelines, the only physical activity outcome to significantly vary by GWG category was the proportion of time spent in MVPA in trimester 2, which was significantly higher amongst women gaining within guidelines than amongst those gaining above or below guidance. Similarly, a US observational study reported that exercising women were more likely to meet GWG recommendations than women who reported no exercise (Harris *et al.*, 2015). In another US study, only VPA, not MPA, was associated with increased odds of gaining

either below or above IOM GWG guidelines amongst women with GDM (Ehrlich *et al.*, 2016). Although it might be expected the women gaining within guidelines may take part in greater MVPA than women gaining in excess of guidelines in the current study, the observation that women gaining below guidelines were taking part in less MVPA than women gaining within guidelines is perhaps unexpected. However, many women experienced pregnancy sickness in the first trimester, which persisted for many women into the beginning of the second trimester. Pregnancy sickness may therefore have influenced both GWG and physical activity in the second trimester.

A systematic review and meta-analysis, published in 2014 suggests that there is limited evidence that physical activity during pregnancy can significantly reduce GWG, but that like the studies described above, research design varies between studies, which makes it difficult to conclude the most successful recommendation for reducing GWG (Elliott-Sale, Barnett and Sale, 2015).

5.4.2.2 Physical activity and infant birth size

Physical activity was not associated with birth weight or infant anthropometrics in any trimester in the present study. In contrast, Hayes et al. (2014) observed a positive association between time spent in sedentary activity at week 36 and infant abdominal circumference, while an inverse association was observed for LPA and MVPA amongst women with obesity. An inverse association was also observed between total energy expenditure in late pregnancy and infant FM, with no relationship observed for FFM nor infant birth weight, in the US Healthy Start Study (Harrod *et al.*, 2014). Performing VPA, as assessed by PPAQ at either 17 weeks or 36 weeks gestation was associated

with decreased birth weight in a small Canadian observational study amongst women of all weights, while only VPA at 17 weeks was associated with decreased FM as assessed by DXA (Bisson *et al.*, 2017). Once again, it is difficult to make direct comparisons between studies, as methods of assessing physical activity, and in this case, infant body composition, have varied between studies, as previously discussed. Studies examining physical activity during pregnancy should measure physical activity objectively, preferably using accelerometry, and ensure that participant wear time is ≥ 720 minutes/day to ensure accurate estimates of physical activity.

5.4.3 **Does the timing and composition of GWG affect infant birth weight and adiposity?**

5.4.3.1 The timing and composition of GWG and birth weight

A moderate positive correlation was observed between rate of maternal FFM accrual and birth weight over total pregnancy and during trimester 2 in the present study, while no associations were observed between rate of maternal FM accrual or GWG and birth weight at any time-point, nor between rate of maternal FFM accrual during trimester 3 and birth weight. These findings are fairly consistent with those observed by Wang et al. (2017) and Farah et al. (2011) who observed positive correlations between maternal FFM, assessed by BIA, and birth weight, in all three trimesters, and at weeks 28 and 37, respectively. Both studies also observed positive associations between total GWG and birth weight, which is in contrast to observations in the present study. These differences can perhaps be explained by methodological differences as these studies included women from all BMI categories, estimated

maternal FFM from BIA rather than from skinfolds, and reported FFM, GWG and birth weight as absolute measurements of mass at single time-points, rather than adjusting for gestational age and reporting as rate of change or as birth weight centile or z-score. The study conducted by Farah et al. (2011) reported the use of segmental BIA which avoided the inclusion of the foetus, amniotic fluid and placenta in body composition analysis. Despite this, the ability of BIA to estimate body composition in pregnancy is compromised as it relies on estimates of TBW, which are influenced by the ratio of intracellular to extracelluar water which vary according to gestational age and is not accounted for in manufacturer-developed equations.

The present study used a maternal SFT equation developed for use in an Australian RCT, conducted by Dodd et al (2015), who did not observe any significant associations between total GWG, percentage body fat, nor individual SFT measurements and infant birth weight. However, unlike the present study, they did not examine for an association between FFM, nor trimester-specific changes in GWG rate. Unlike BIA, the SFT equation used in the current study and Dodd et al. (2015) does not rely on estimates of TBW, and assumes that changes in upper-body subcutaneous fat are proportional to TBF, as the SFT sites in the equation are not areas thought to be influenced by foetal growth. Remaining GWG is therefore assumed to be FFM and incorporates TBW, the foetus, placenta and amniotic fluid, which is likely to explain the positive association between rate of maternal FFM accrual and infant birth weight in the present study. Butte et al. (2003) estimated maternal body composition from a four compartment model in 63 women, and observed positive associations between

birth weight and GWG, rate of GWG and gain in FFM, but not FM. FFM gains in each of the three trimesters were also positively associated with birth weight as were changes in TBW in the second and third trimesters, and changes in total body potassium in the third trimester.

Despite methodological differences between the studies described above and in the present study, maternal FFM appears to play an important role in the predication of infant birth weight. Further studies using methods of assessment that are able to distinguish between the maternal and foetal unit are warranted, although achievement of this is likely to require the use of four-compartment models, which is not generally feasible in larger cohort studies. Widen and Gallagher (2015) suggest further validation of portable methods such as BIA is required with revised equations for use in pregnancy to account for changes in TBW and FFM hydration during pregnancy.

5.4.3.2 The timing and composition of GWG and infant body composition

As previously described, infant UME and UFE were estimated and used as proxies for infant FFM and FM, respectively. Once again, rate of maternal FFM accrual during trimester 2 and over total pregnancy were positively associated with infant UME, but not triceps skinfold nor UFE. There were no associations observed between GWG nor rate of maternal FM accrual and infant body composition, which is in contrast to several other studies, which observed a positive correlation between total GWG and infant FM and FFM (Carlsen *et al.*, 2014; Starling *et al.*, 2015) as well as trimester-specific GWG and infant FM (Davenport *et al.*, 2013) and FFM (Starling *et al.*, 2015). As

part of the Healthy Start study, Starling et al. (2015) observed a positive association between rate of GWG over pregnancy and infant FM, FFM and percentage FM, as well as a positive association between early-, mid- and late-pregnancy GWG and infant FM, and mid-and late-pregnancy GWG and infant FFM. These studies used different methods to estimate infant body composition such as PeaPod ADP (Starling *et al.*, 2015), TOBEC (Davenport *et al.*, 2013) and DXA (Carlsen *et al.*, 2014) which as mentioned previously, are more direct measures of body composition than those used in the present study, and could in part reflect the conflicting findings. In keeping with the present study, the Norwegian STORK study used SFT measurements to assess infant subcutaneous fat. Mid-pregnancy rate of GWG (15-28 weeks gestation) was the strongest independent predictor of infant sum of SFT (Sommer *et al.*, 2015), although unlike the present study, no proxy for infant FFM was used.

No studies appear to have examined the relationship between the rate at which maternal body composition changes over pregnancy and infant body composition, so there is no data to compare directly to the observations in the present study. However, given the likely potential relationship observed between maternal FFM and infant birth weight, further studies should examine the relationship between the composition of GWG and infant body composition.

5.4.3.3 Institute of Medicine gestational weight gain guidelines and infant birth size

In the present study, no differences between IOM groups were observed for any infant birth weight or body composition outcomes. This is not surprising, as the sample was not powered to examine for these differences. However, it is important to

acknowledge that other, larger studies have observed significantly greater odds of LGA or macrosomia amongst women gaining in excess of IOM guidelines in both normal weight and women with obesity (Vesco *et al.*, 2011; Alberico *et al.*, 2014; Goldstein *et al.*, 2017). GWG in excess of IOM guidelines has also been associated with increased infant FM for women of all weights (Crozier *et al.*, 2010), women of normal weight, but not women with obesity (Waters, Huston-Presley and Catalano, 2012; Henriksson *et al.*, 2015) and for women with overweight and obesity only (Hull *et al.*, 2011). Although findings of these studies have varied, for now, they suggest that women should be encouraged to adhere to the IOM guidelines as they appear to positively influence infant birth weight and adiposity.

5.5 Conclusion

The present study suggests that as expected, maternal EI is associated with GWG and rate of FM accrual in the second and third trimesters. In the third trimester only, rate of GWG was positively associated with energy from CHO and sugar and both rate of GWG and rate of FM accrual were inversely associated with energy from protein. While the proportion of energy from sugar in trimester 3 was also significantly and positively associated with infant birth weight and UME, it was maternal rate of FFM accrual, not FM nor rate of GWG (in both trimester 2 and over total pregnancy) that were positively associated with infant birth weight and UME. These findings suggest that maternal interventions amongst women with obesity should perhaps focus on encouraging women to limit their sugar intake to limit GWG, maternal FM accrual and improve infant birth size outcomes. Previous work has shown that increased GWG and

FM accrual is associated with increased infant birth weight and postpartum weight retention (PPWR; Butte *et al.*, 2003; Siega-Riz *et al.*, 2009). However, as the present study and current literature suggests maternal FFM as a predictor of infant birth size, it is not clear how, or indeed if, interventions should address changes in maternal body composition over pregnancy, or if they should continue to focus on limiting total GWG.

Chapter 6 **General Discussion**

The proportion of women entering pregnancy with overweight or obesity is increasing in the UK, which means that more women are presenting at UK antenatal clinics with obesity. Obesity during pregnancy, and excessive GWG, particularly amongst women with obesity, increase the risk of numerous adverse consequences for both mother and baby (Scott-Pillai *et al.*, 2013; Goldstein *et al.*, 2017), particularly in relation to infant birth size. The timing and composition of GWG, and their influence on infant anthropometric measurements, are less well understood, with little research amongst British women. The present study has attempted to observe the effect of maternal diet and physical activity on the timing and composition of GWG, as well as on infant body composition. The study is the first, to our knowledge that has examined the impact of maternal diet and PA on trimester-specific rates of GWG, FM and FFM accrual, and the effect of these maternal GWG outcomes on infant anthropometric measurements in the UK.

6.1 Summary of observations

A summary of the main findings from the study can be seen in Figure 6.1.

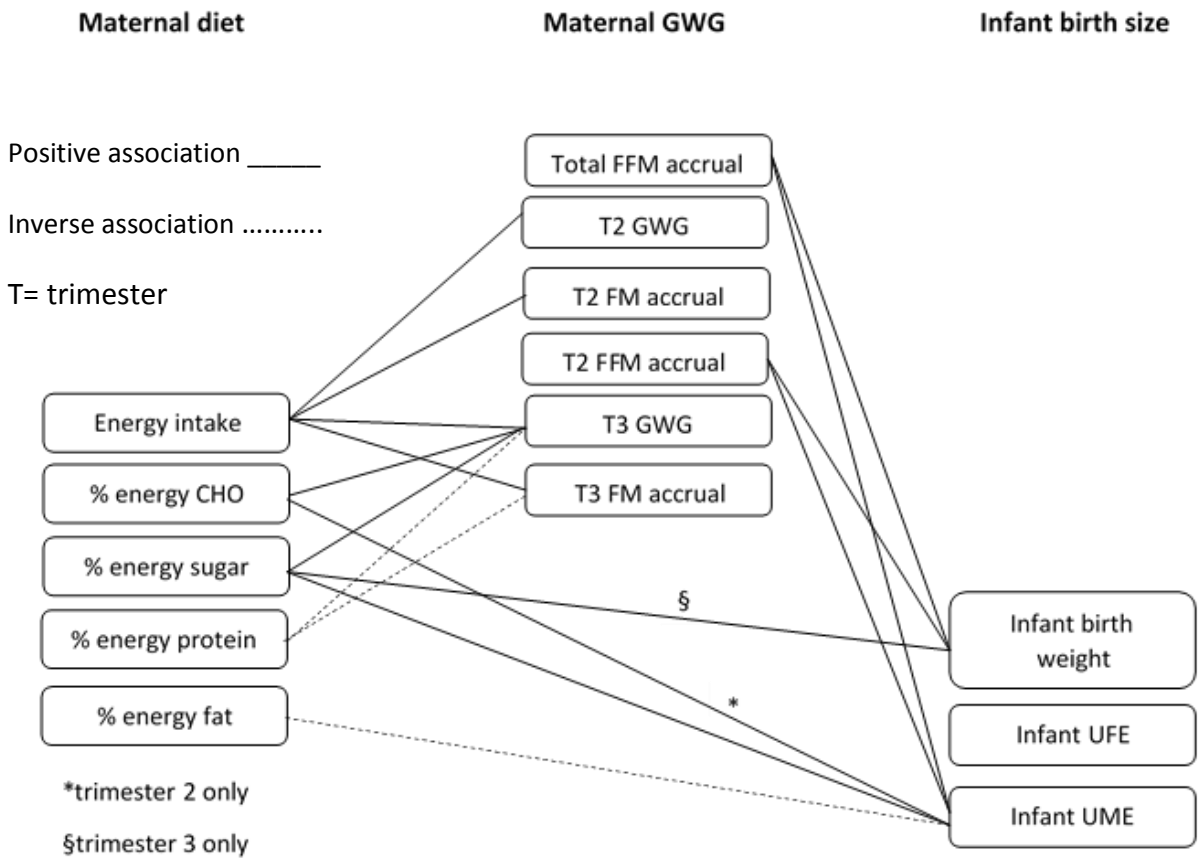


Figure 6.1 Summary of observations

6.2 Implications of the findings

The assessment of the timing and composition of GWG is important within a UK setting, as there are currently no British GWG guidelines, and women are not routinely weighed as part of their antenatal care. The present study estimated trimester-specific rates of total GWG, FM accrual and FFM accrual, how these outcomes are influenced by maternal diet and activity, and how they in turn influence infant birth size. Although previous studies have examined the rate of maternal GWG, to the best

of the author's knowledge, the present study is the first to estimate trimester specific rates of GWG, FFM and FM accrual amongst a UK population. Examining the changes in GWG, FFM and FM in this manner may improve our understanding of how maternal lifestyle interventions during pregnancy may influence changes in maternal body composition, which may in turn influence other maternal and infant outcomes. Findings from the present study suggest that infant birth weight is more strongly influenced by maternal rate of FFM accrual than rate of GWG or FM accrual, which is in agreement with previous work examining maternal body composition as absolute measurements of mass rather than rate of accrual (Butte *et al.*, 2003; Farah *et al.*, 2011; Kent *et al.*, 2013; Wang *et al.*, 2017).

Unsurprisingly, maternal EI was positively associated with both rate of GWG and FM accrual in both trimesters 2 and 3 and in trimester 3 only, positive associations were observed for energy from CHO and sugar, and inverse associations for protein, which again, agreed to some extent with previous work (Olafsdottir *et al.*, 2006; Diemert *et al.*, 2016). Excessive GWG and FM accrual, are known to be associated with PPWR, which increases the risks of obesity and related chronic disease. Current advice for women is to increase their energy intake by 191 kcal in the third trimester only (Scientific Advisory Committee on Nutrition, 2011). However, this advice is based on EARs so half the population will require a greater increment, and half a lower increment. The third trimester energy increment is also based on the assumption that women are adhering to EARs prior to pregnancy, and that they are weight stable prior to pregnancy, which is not known for the women in the present study.

Practically, and in order to avoid excessive GWG, the only way for health professionals to advise women on their diet and energy intakes is to perhaps reintroduce regular weighing of women throughout pregnancy.

Interestingly, maternal diet was not associated with rate of FFM accrual at any time-point, so although maternal FFM accrual seems to be an interesting potential predictor of infant birth size, it is not clear how maternal diet may influence rate of FFM accrual, and to our knowledge, this has not been examined elsewhere.

On the other hand, proportion of energy from sugar in the diet was positively associated with infant UME in both trimesters 2 and 3, and in trimester 3 only, energy from sugar was also positively associated with infant birth weight z-score. However, whether this sugar was coming from naturally occurring sources, or from free sugars can not be ascertained from the present study, and future studies should examine intakes of free sugars in greater detail during pregnancy, or this could suggest a further role for DPA in order to identify the types of foods containing sugars associated with infant birth size outcomes. Inverse associations were also observed between trimester 2 and 3 percentage energy from fat and infant UME. Previous studies have suggested associations between maternal diet and infant birth weight and FM (Renault *et al.*, 2015; Crume *et al.*, 2016), but not FFM. Maternal energy and CHO intakes in particular appear to influence infant birth size, but in which direction, it is not clear (Godfrey *et al.*, 1996; Knudsen *et al.*, 2013). Further work should focus on distinguishing between types of CHO, as well as GI and GL of the diet during pregnancy.

Findings from the present study therefore suggest that maternal EI and macronutrient composition influence both the timing and composition of GWG and may also influence infant birth size. The present study is, however, unable to explore any further for an interaction between diet, the timing and composition of GWG and infant birth size due to sample size limitations, and as explained below, is already underpowered to identify some associations between maternal and infant outcomes.

6.3 Limitations

Like all research, the current study is not without its limitations, and these should be considered when interpreting the results.

6.3.1 **Sample size**

The primary limitation of the study is the sample size of just 75 women. The original sample size calculation revealed that in order to detect a simple correlation between GWG, and birth weight, with a medium effect size of 0.3 and power of 80%, 82 participants were required. In order to account for an attrition rate of approximately 15%, the researcher was aiming to recruit 97 participants.

Although this target was exceeded, dropout between recruitment and consent was higher than anticipated, and it was not possible to extend the recruitment phase any further due to lack of time and resources, with just one researcher responsible for recruiting and visiting women throughout the study.

Just 31% of women approached consented to participate in the study, and thus there is a possibility of selection bias as women who volunteered to participate in the study may not be representative of all pregnant women with obesity in Plymouth (Hammer,

Prel and Blettner, 2009). Information was not available on the characteristics of non-participants; however, the researcher felt that women who volunteered to participate were perhaps more interested in leading a healthy pregnancy than those who refused. Nonetheless, as discussed previously, women participating in the study came from all areas of Plymouth and appear to be demographically similar to women nationally in the UK.

Of the 75 women who enrolled in the study, 16% were lost to follow up by the third and final maternal visit to collect anthropometric data, which was similar to the attrition rate of 15% that was expected based on previous studies. However, compliance with the collection of dietary data and accelerometry was considerably lower than compliance with anthropometric measurements, with just 34 women (45%) completing the study in full.

Findings from the study should therefore be interpreted cautiously, and some of the statistical analysis performed was not adequately powered. Having said that, the original power calculation was based on a simple correlation between total GWG and birth weight, for which no association was observed in the present study. Whether this was because the study was not powered to detect a small effect of total GWG on birth weight, or whether the association is not there, cannot be said. However, as the current study is the first, to the author's knowledge, to examine the effect of the rate of accrual of FM and FFM on birth weight and infant body composition, there was no data on which to base an *a priori* power calculation. Posthoc power calculations show that the larger effect sizes observed for the effect of rate of FFM accrual on birth

weight in fact reached 80-97% power, although the effect of FFM on infant UME was underpowered at just 65%. The study was not powered to examine for differences between groups, for example, those who developed GDM and those who did not, or between IOM GWG groups. In some cases, analyses were still performed, despite being underpowered, for completion of the work, but these findings must be interpreted particularly cautiously.

6.3.2 **Gestational weight gain data**

Women were not approached to participate in the current study until their 12 week dating scan at antenatal clinic, and as such, GWG and maternal body composition data was not collected until the end of the first, or beginning of the second trimester. As such, the current study does not have any maternal weight or body composition data prior to conception or during the first trimester, which is common to other studies, which typically recruit at the end of the first trimester, once a scan has confirmed a viable pregnancy. This is a major limitation of the current study and other comparable studies in the literature as it has been shown that the periconception period plays an important role in foetal growth and development (Ravelli, Stein and Susser, 1976; Van Dijk *et al.*, 2017).

However, due to practicalities surrounding recruitment it is very challenging to recruit eligible women to a study of this nature prior to 12 weeks gestation. Until their dating scan women in the UK attend antenatal appointments at various locations in the community, and these appointments occur at different stages of gestation for each woman, depending on the gestation at which they discover they are pregnant. A

recent report states that in England, of women with known booking dates, 38.8 % booked at 9 weeks or less, while a further 39.3 % of women booked between 10 and 12 weeks gestation, inclusively (Health and Social Care Information Centre, 2017) . Attempting to recruit women any earlier than 12 weeks decreases the proportion of eligible women who can be approached and also increases the risk of inclusion bias. A way round this would be to recruit women receiving fertility treatment prior to conception, but these women are not likely to be representative of the reproductive population as they may have already implemented lifestyle changes in order to increase their chance of conceiving (Homan, Davies and Norman, 2007).

The final maternal anthropometric measurements were collected at the end of the third trimester, at 36 weeks gestation. This time-point was chosen in order to reduce the chance of missing the opportunity to obtain a final maternal set of measurements, as it is common for women with obesity and/or GDM to be induced at 37 weeks gestation (Cnattingius *et al.*, 2013). However, some women remained pregnant for up to 6 weeks after this final measurement was taken and may therefore have experienced subsequent changes to their weight and/or body composition during this time, which cannot be accounted for in the present study.

In order to attempt overcome these limitations of 'missing' early and late pregnancy weight and body composition data, rate of change for GWG, FM and FFM has been reported. Estimates of FM and FFM were obtained at the end of each trimester of pregnancy from an equation using SFT measurements from the biceps, triceps and subscapular, AC and height (Kannieappan *et al.*, 2013). Although this equation has

been previously validated amongst pregnant women with obesity, the use of SFT equations does introduce an additional level of error and this does limit the extent to which data from the present study may be compared with that of others.

6.3.3 **Dietary data**

The accuracy and reliability of the dietary data is another potential limitation of the study. Compliance with the collection of dietary data was poorer than that of the anthropometric data, with 88%, 77% and 69% of women completing diet diaries at study visits 1, 2 and 3, respectively. Dietary data was therefore missing for some women, which may have resulted in non-response bias. The prospective nature of the food diary may also have caused participants to alter their eating habits and thus created an observation bias. However, collecting dietary data retrospectively, for example, via 24 hour recall could also introduce recall bias.

Participants were asked to give as much information regarding their portion sizes as possible, and encouraged to include packaging, weights from packaging, photos and household measurements where possible. However, the researcher was often required to estimate portion sizes, which was performed where possible using information from manufacturers or retailers. Where this was not possible, 'Food Portion Sizes' was used to estimate portion sizes (Mills and Patel, 2002). However, this book has not been updated since 2002, and population average portion sizes have been shown to be increasing (Steenhuis, Leeuwis and Vermeer, 2010). Many foods consumed by women were not in the book, nor were they present in the nutrient analysis software database. Again, where possible the researcher used packaging and

information from manufacturers and retailers to obtain nutritional information, which was often missing for key nutrients, or a similar food was chosen from the database. This introduced potential random error. These limitations could potentially have been overcome by asking participants to weigh their food intake. However, compliance was already lower for this arm of the study, and placing additional burden on participants may have increased study attrition further.

As with any study examining dietary intake, the possibility that participants have mis-reported their dietary intake must be taken into account. As previously discussed, mean values for EIs across all three trimesters were considerably lower than EARs, suggesting that at least some of the women in the study under-reported their food intake. Previous studies amongst pregnant women suggest that a Goldberg ratio <0.9 is a sign of 'definite reporting' (McGowan and McAuliffe, 2012). In the current study, 26, 28 and 21% of women had a Goldberg ratio <0.9 in trimesters 1, 2 and 3. However, it was not felt that women with an EI:BMR <0.9 could be removed from analysis with certainty that their lower food intake was not as a result of pregnancy sickness (in the first trimester), or as a result of altering their food intake in response to a GDM diagnosis (at the end of the second trimester or during the third). Dietary data was therefore retained for analysis for all women, so there is a large probability that at least some of the women under- or mis-reported their food intake. Previous research has shown a positive association between BMI and under-reporting, particularly amongst women (Macdiarmid and Blundell, 1998). Under-reporters have also been shown to particularly under report intakes of carbohydrate and fat, as well as snacks

between meals. Whether there was under-reporting of portion sizes, or of specific foods or nutrients cannot be determined from the data in the present study, so this data should be interpreted with caution.

6.3.4 **Physical activity data**

Compliance with the accelerometry component of the study varied over the three trimesters with just 51% of the cohort completing at least three days of accelerometry in all three trimesters. This is a limitation as it may introduce potential non-response bias if those who did not complete accelerometry differed in their levels of activity compared to compliers. The present study identified particularly high levels of physical activity amongst the cohort. Mean time spent in MVPA/day exceeded weekly UK recommendations and observations in other studies (Kinnunen *et al.*, 2011; Hayes *et al.*, 2014), which raised the question of device error, experimenter error or poor choice of epoch or cut-points. Data has been checked, reanalysed and cut-points and epochs were chosen to enable comparison with other studies: no errors could be identified. The only discrepancy that can be identified was that WT was considerably higher amongst women in the present study compared with others, which could explain the considerably higher levels of physical activity observed.

6.3.5 **Infant birth size data**

Infant birth weight and head circumference were obtained from hospital notes, and thus rely on the accuracy, reliability and validity of hospital apparatus and technical expertise of hospital staff. Infant birth length, AC and triceps skinfold measurements were obtained by a single researcher, using the same apparatus, which eliminated

inter-observer error but not measurement error. Infant AC and triceps SFT measurements were used to estimate infant UME and UFE from a previously validated equation (Rolland-Cachera *et al.*, 1997). However, the limitations of UFE and UME must be acknowledged as just proxies for infant FM and FFM which assume the composition of the arm is representative of the whole body. The gold standard tool for the assessment of newborn body composition is the PeaPod ADP device (Ellis *et al.*, 2007) which was not available during the present study due to the lack of availability in Plymouth and lack of funds to purchase one. To our knowledge, no studies in the UK examining maternal GWG and body composition have used PeaPod ADP to assess infant body composition. Given the potential association identified in the current study between maternal FFM accrual and infant UME, future studies should incorporate the use of ADP in order to assess infant body composition with greater accuracy and validity.

6.4 Recommendations

The present study is not large enough for the conclusions drawn from it to warrant changes to antenatal care. However, given the potential role of the timing and composition of GWG on infant birth size, the introduction of regular weighing of women throughout their pregnancy should perhaps be considered. Routine weighing of women during pregnancy has been a topic of much debate in the UK (Oken, 2015; Steer, 2015), and at present, NICE conclude that there is insufficient evidence on which to base recommendations (National Institute for Health and Care Excellence, 2010). Recent studies have suggested that lifestyle interventions do have the potential to

significantly reduce excessive GWG (Phelan *et al.*, 2011; Rauh *et al.*, 2013), however, findings have not been applied to routine antenatal care. A RCT is currently being conducted in the UK to determine the effectiveness of a brief intervention embedded within antenatal care at reducing GWG (Daley *et al.*, 2016). The results from the present study suggest that FFM accrual may influence infant birth size more strongly than GWG. However, without routine weighing, the assessment of changes to maternal body composition will not be possible, and further work is required to examine the influence of maternal body composition on maternal and infant outcomes.

Findings from the present study suggest that women with obesity in Plymouth were exceeding DRVs for the proportion of energy from saturated fat. Energy intake was also positively associated with GWG and FM accrual which is known to contribute to PPWR. As previously discussed, dietary guidelines during pregnancy, particularly for energy, are based on estimated requirements and generally assume that women are weight-stable and adhering to EARs pre-pregnancy. Personalised dietetic support alongside regular weighing has been shown to help women to adhere to personalised dietary advice based on their pre-pregnancy weight, and also to reduce the risk of excessive GWG (Robertson and Ladlow, 2017; Sagedal *et al.*, 2017). At present, there is not the capacity within the NHS to offer such personalised dietetic support for women with obesity and any attempt to provision such a service will increase the cost for the NHS in the UK. However, as previously stated, it is estimated that obesity during pregnancy costs an average an average of £2310 extra from conception to infant's first

birthday, and that interventions costing less than this would be cost-effective (Morgan *et al.*, 2015).

Research has shown that although open to the idea of providing weight management advice to women with obesity during pregnancy, many midwives lack the confidence, expertise and time within their workload to offer this (McCann *et al.*, 2017). Hazeldine et al. (2016) highlight the potential importance of the inclusion of a psychological dimension into pregnancy lifestyle interventions in order to increase their efficacy. This is supported by the success of multi-disciplinary approaches to antenatal care which have improved various maternal and foetal outcomes with the involvement of clinical psychologists and/or psychological theory to promote behaviour change (Quinlivan, Lam and Fisher, 2011; Poston *et al.*, 2015). In Plymouth, women with a BMI $\geq$ 35 kg/m^2 are now being offered the opportunity to attend group antenatal care sessions, which alongside routine antenatal care, provides women with sessions on diet and lifestyle choices during pregnancy, and also includes a weekly pregnancy exercise class. This is a pilot project and data from the service is currently under audit, and whether there would be scope, adequate staffing and funds for roll-out across the city of Plymouth is unclear at present.

6.5 Future research

The present study has identified areas that require further detailed investigation, in particular the impact of the rate of change in maternal body composition on infant birth size. The main limitation of the present study was its small sample size, and therefore it would be particularly valuable to conduct a similar study on a larger scale.

A larger study could be adequately powered to detect smaller effects and could include women of different ethnicities and in different geographic areas of the UK. A larger sample size would also enable regression analysis in order to examine for interactions between maternal lifestyle, timing and composition of GWG and infant birth size.

The present study focussed on women with obesity with a BMI between 30 and 40 kg/m^2. These women were chosen as previous studies have shown that women with obesity are at increased risk of adverse pregnancy outcomes, and the study was not adequately powered to detect differences between women in different BMI categories, so women in this BMI group were chosen to provide a more homogenous sample. Including women of all BMIs in a larger cohort study would enable the observation of rate of GWG, FM and FFM accrual across pregnancy in women of all weights, which again, to our knowledge has not been described in this way in a UK cohort.

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10.1007/s00125-006-0422-1.

Appendix 1 – NHS Health Research Authority ethical approval

Health Research Authority

National Research Ethics Service

NRES Committee London - Central
3rd Floor, 4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7821
Fax:0161 625 7299

17 September 2014

Miss Kathy Redfern
B409 Portland Square
Drake Circus
Plymouth
PL4 8AA

Dear Miss Redfern

Study title:	**The effects of the timing and composition of gestational weight gain, dietary intake and energy balance on neonatal anthropometric outcomes in an obese obstetric population in the UK.**
REC reference:	**14/LO/1660**
IRAS project ID:	**153479**

Thank you for your email, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the Chair and Mr Clive Carsley.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the REC Manager, Miss Shehnaz Ishaq, NRESCommittee.London-Central@nhs.net

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations

involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Covering letter on headed paper [Covering Letter]	1	10 August 2014
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Evidence of Insurance]	1	07 August 2014
GP/consultant information sheets or letters [GP Information Letter]	1	14 July 2014
IRAS Checklist XML [Checklist_01092014]		01 September 2014
Letter from statistician [Sample Size Calculation]	1	23 May 2014
Letters of invitation to participant [Letter of Invitation]	1	18 July 2014
Participant consent form	2	02 September 2014
Participant information sheet (PIS)	2	02 September 2014
REC Application Form [REC_Form_01092014]		01 September 2014

Referee's report or other scientific critique report [Independent Commentator Report]	1	02 July 2014
Research protocol or project proposal [Project Protocol]	1	07 August 2014
Summary CV for Chief Investigator (CI) [Summary CV for Kathy Redfern]	1	07 August 2014
Summary CV for supervisor (student research) [Summary CV for Gail Rees]	1	14 July 2014
Summary, synopsis or diagram (flowchart) of protocol in non-technical language [Protocol Summary]	1	07 August 2014

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

14/LO/1660	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Signed on behalf of:
Dr Andrew Hilson
Chair

Email: NRESCommittee.London-Central@nhs.net

Enclosures:	“After ethical review – guidance for researchers”
Copy to:	Dr Gail Rees
	Dr Lisa Vickers, Plymouth Hospitals Trust R&D

Appendix 2 – Plymouth NHS Hospitals Trust R&D ethical approval

Plymouth Hospitals NHS
NHS Trust

Dr Ross Welch
Consultant in Fetomaternal Medicine
Derriford Hospital
Plymouth
PL6 8DH

Research & Development Office
Room N17, ITTC Building
Derriford
Plymouth
PL6 8BX

Tel: (01752) 432197/432196
Fax: (01752) 315 110

06/11/2014

Dear Dr Welch

Re: NHS R&D Permission for research project

Eudract: **NA**
MREC: **14/LO/1660**
UKCRN: **NA**
R&D ref: **14/P/134**

Study title: The effects of the timing and composition of gestational weight gain, dietary intake and energy balance on neonatal anthropometric outcomes in an obese obstetric population in the UK

This letter confirms that the study named above has Plymouth Hospitals NHS Trust R&D permission to proceed. The governance review carried out included the following documents:

Document	Version	Document Date
Protocol	1	7 August 2014
Participant Information Sheet	2	15 September 2014
Consent Form:		
Main	3.0	10 October 2014
Maternal and cord blood samples	3.0	10 October 2014
GP Letter	1	14 July 2014
Patient Invitation letter	1	18 July 2014

Note: R&D approval extends to all documents that have received a favourable ethical opinion from the relevant Research Ethics Committee, whether or not they have been referenced in this letter.

Please note that the Trust's funding is contingent upon research studies recruiting their first patient within 30 calendar days of R&D permission. We therefore encourage you to be in a position to recruit as soon as possible.

Yours sincerely

L M Vickers

Dr Lisa Vickers
R&D Manager

Appendix 3 – Patient Information Leaflet

We would like to invite you to take part in a study looking at your diet, exercise and weight gain during pregnancy and their effect on the size of your baby when its born. The study will form part of a PhD qualification at Plymouth University. Recent studies have suggested that weight gain during pregnancy influences birth weight and body composition of babies at birth and during their first few months. To our knowledge, this will be the first study of its kind. It is hoped that results from this study will help to influence pregnancy guidelines in the future.
We understand that you may have some questions about this research. Below are some common questions and answers.

Who has approved this project?
This study has been approved by the NHS Research Ethics Committee (Ref: 14/LO/1660), as well as Plymouth NHS Hospitals Trust Research & Development Department (Ref: 14/P/134).

Is my participation voluntary?
Yes

Will my care be compromised if I decide not to take part in this study?
No, you will receive the same care regardless of whether you choose to take part.

Why have I been chosen to take part?
All pregnant women in your area with a body mass index greater than 30 and who are less than 12 weeks pregnant have been asked to take part in this study.

What would be involved in taking part in this study?
You would be asked to meet with the researcher at the following times during your pregnancy, and once your baby is born. Please note, the researcher will meet you wherever and whenever is most convenient for you e.g. at home after work.

- At week 12, 28 and 37 of your pregnancy:
The researcher would ask to take your weight and body composition measurements. Your body composition will be estimated using skinfold callipers which measure the thickness of a fold of your skin at three sites on your body: the front (biceps) and back (triceps) of your arms, and over your shoulder blade (subscapula). You would also be asked to complete a 4 day diet diary and wear an accelerometer during this period. An accelerometer is a small device much like a pedometer, worn on your wrist, that measures your physical activity. At the end of the 4 day period the researcher would return to collect your data.

-Within 3 days of your baby's birth:
The researcher would ask to visit you and your baby within 3 days of birth (either at hospital or at home) in order to measure your baby's length, arm circumference, and to take two skinfold measurements at the triceps and subscapula. This will take less than 15 minutes.

-Access to notes:
The researcher would ask to have access to your hospital records in order to determine when you have given birth and to record your baby's birth weight, head circumference and any details relevant to the study such as any illnesses experienced during your pregnancy, or any interventions performed during your labour.

We hope to build on this research project and obtain ethical approval for a future study. With your additional consent we would therefore like to collect the following blood samples which would be analysed to examine genes associated with body weight at a later date.

- The collection of a blood sample at the same time as you have a routine blood test as part of your pregnancy.
- The collection of a sample of cord blood from your baby's placenta. This would occur after your baby's birth, once you have delivered the placenta and your baby's umbilical cord has been cut.

What if I change my mind?
You can withdraw from this study at any point without having to give an explanation. This will have no effect on the care you receive.

Will taking part be of any benefit to me?
Perhaps not directly, however, we hope that this study will help to influence and improve care during pregnancy in the future.

Are there disadvantages to taking part?
We recognise that taking part will take up a little of your time. However, we will do our best to minimise any inconvenience by ensuring research is conducted at a time and location to suit you.

Will my participation be confidential?
Yes, all data will be completely anonymous.

How long will you keep my data?
We will need to keep your data on file for 3 years after the study has ended.

What will you do with the data?
We plan to publish the results of the study in academic and professional journals in order to inform the care women receive during pregnancy. There will be the opportunity for you to receive a brief report of the main study findings at the end of the research.

I have further questions:
If you have any further questions about the project please feel free to contact the research team or the ethics team using the contact details on the back of this leaflet.

Thank you for reading this leaflet and for considering being part of this study.

Researcher:
Kathy Redfern
School of Biomedical and Healthcare Sciences
Plymouth University
kathy.redfern@plymouth.ac.uk

Supervisor:
Dr Gail Rees
School of Biomedical and Healthcare Sciences
Plymouth University
gail.rees@plymouth.ac.uk
01752 584647

Plymouth NHS Hospitals Trust Research & Development Office:
Email: plh-tr.RD-Office@nhs.net
Tel: 01752 432 197

This project is part of a postgraduate degree requirement.

The normal NHS complaints mechanism is available to you if you wish to complain about any way you are approached or treated during this project.

Version 2 : 15/09/14

Plymouth Hospitals NHS
NHS Trust

RESEARCH WITH PLYMOUTH UNIVERSITY

Weight gain, diet and activity during pregnancy: how does this affect your baby's size at birth?

PARTICIPANT INFORMATION LEAFLET

Leading with excellence, caring with compassion

Appendix 4 – Participant Consent Form

Plymouth Hospitals NHS
NHS Trust

RESEARCH WITH PLYMOUTH UNIVERSITY

Consent Form

Participant Number:

Title of Project: Timing and composition of weight gain, diet and physical activity during pregnancy and the impact on infant birth weight and body composition.

Name of Researcher: **Kathy Redfern**

Please initial or tick the boxes below.

1. I confirm that I have read the information sheet dated. 11/09/14 (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by the researcher (Kathy Redfern) where it is relevant to my taking part research. I give permission for this individual to have access to my records. ☐

4. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers. ☐

5. I agree to my GP being informed of my participation in the study. ☐

6. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

Appendix 5 – Data collection sheet - baseline

Participant Information at Baseline.

Subject Number:	☐ Consent for blood samples?	Date: __/__/__

RESEARCH WITH PLYMOUTH UNIVERSITY

Date of Birth: _____ / ____ / _____ Age at study entry: _____

Date of LMP _____/_____/_____ Occupation: _____

Due date: _____ / ____ / _____ Ethnicity: _____

Week 12 _____ / ____ / _____ Maternal bloods date: _____ / ____ / _____

Week 28: _____ / ____ / _____

Week 36 _____ / ____ / _____

☐ Midwife-led care?

Name of midwife: _____

☐ Consultant-led care?

Name of consultant: _____

Pre-pregnancy weight: _ _ _ _ _ _ _ _

Is this your first pregnancy? ☐ Yes ☐ No How many other children do you have? _ _

Do you smoke? ☐ Yes ☐ No

If yes, do you plan to continue smoking during your pregnancy? ☐ Yes ☐ No

Do you use E-Cigarettes? ☐ Yes ☐ No

If yes, do you plan to continue using them during your pregnancy? ☐ Yes ☐ No

Approximately how many units of alcohol do you drink per week? _ _ _ _

Did you take a folic acid supplement prior to conception? ☐ Yes ☐ No

Have you been taking folic acid supplements during your 1st trimester? ☐ Yes ☐ No

Have you experienced morning sickness so far? ☐ Yes ☐ No

If yes, has your appetite been affected? ☐ Yes ☐ No

Participant Information at Baseline.

How would you like to be contacted about this study? (please tick all that apply)

☐ Telephone call.

Telephone number: _

☐ Text message

Mobile phone number: _

☐ Email

Email address: _

Where would you like your measurements to be taken?

_____

Address:

_____

_____

Where would you prefer for your baby's measurements taken?

☐ Same as above ☐ Labour ward ☐ Other:

Who is your GP? _____

Surgery: _____

Address:_____

_____

Any other notes?

_____

_____

_____

_____

_____

Appendix 6 – Data collection sheets: visits 1-3

Study visit 1, 2 and 3 data collection sheet

Subject Number:

RESEARCH WITH PLYMOUTH UNIVERSITY

Date:

Gestation:

Anthropometry:

Weight: _____ BMI at booking: _____

Height: _____ _____ _____

Arm circumference: _____ _____ _____

Triceps Skinfold: _____ _____ _____

Biceps Skinfold: _____ _____ _____

Subscapular Skinfold: _____ _____ _____

Energy Balance:

Diet diary & Accelerometer Wear: _____

Notes:

Appendix 7 – Study diet diary

Weight gain, diet and activity during pregnancy: how does this affect your baby's size at birth?

4 Day Food Diary

Subject ID:

Start Date:

RESEARCH WITH PLYMOUTH UNIVERSITY

PLEASE READ THROUGH THESE PAGES BEFORE STARTING YOUR DIARY

We would like you to keep this diary of <u>everything you eat and drink</u> over 4 days. Please include all food consumed at home and outside the home e.g. work, college or restaurants. It is very important that you do not change what you normally eat and drink just because you are keeping this record. Please keep to your usual food habits.

<u>Day and Date</u>
Please write down the day and date at the top of the page each time you start a new day of recording.

<u>Time Slots</u>
Please note the time of each eating occasion into the space provided. For easy use each day is divided into sections, from the first thing in the morning to late evening and through the night.

<u>Where and with whom?</u>
For each eating occasion, please tell us what **room or part of the house** you were in when you ate, e.g. kitchen, living room, If you ate at your work canteen, a restaurant, fast food chain or your car, write that location down. We would also like to know **who you share your meals with**, e.g. whether you ate alone or with others. If you ate with others please describe their relationship to you e.g. partner, children, colleagues, or friends. We would also like to know **when you ate at a table** and **when you were watching television whilst eating**. For those occasions where you were **not** at a table or watching TV please write 'Not at table' or 'No TV' rather than leaving it blank.

<u>What do you eat?</u>
Please describe the food you eat in as much detail as possible. Be as specific as you can.

- **<u>Homemade dishes</u>**
  If you have eaten any **homemade dishes** e.g. chicken casserole, please record the name of the recipe, ingredients with amounts (including water or other fluids) for the whole recipe, the number of people the recipe serves, and the cooking method. Write this down in the recipe section at the end of the record day. Record how much of the whole recipe you have eaten in the portion size column (see examples on pages 4 - 15).

- **<u>Take-aways and eating out</u>**
  If you have eaten **take-aways** or **made up dishes not prepared at home** such as at a restaurant or a friend's house, please record as much detail about the ingredients as you can e.g. vegetable curry containing chickpeas, aubergine, onion and tomato.

<u>Brand name</u>
Please note the **brand name** (if known). Most packed foods will list a brand name, e.g. Bird's eye, Hovis, or Supermarket own brands.

- ***Labels/Wrappers***

Labels are an important source of information for us. It helps us a great deal if you enclose, in the plastic bag provided, labels from all **ready meals,** labels from **foods of lesser known brands** and also from any **supplements** you take.

Portion sizes

For foods, quantity can be described using:

- **household measures**, e.g. one teaspoon (tsp) of sugar, two thick slices of bread, 4 tablespoons (tbsp) of peas, ½ cup of gravy. Be careful when describing amounts in spoons that you are referring to the correct spoon size. Compare the spoons you use with the life size pictures on page 28 of this diary.
- **weights from labels**, e.g. 4oz steak, 420g tin of baked beans, 125g pot of yoghurt
- **number of items**, e.g. 4 fish fingers, 2 pieces of chicken nuggets, 1 regular size jam filled doughnut
- **picture examples** for specific foods on pages 22-24.

For drinks, quantity can be described using:

- the **size of glass, cup etc** (e.g. large glass) or the **volume** (e.g. 300ml).
- **volumes from labels** (e.g. 330ml can of fizzy drink).

We would like to know the **amount that was actually eaten** which means taking **leftovers** into account. You can do this in two ways:

1. Record what was served and make notes of what was not eaten e.g. 3 tbsp of peas, only 2 tbsp eaten; 1 large sausage roll, ate only ½
2. Only record the amount actually eaten i.e. 2 tbsp of peas, ½ a large sausage roll

Was it a typical day?

After each day of recording you will be prompted to tell us whether this was a typical day or whether there were any reasons why you ate and drank more or less than usual.

Supplements

At the end of each recording day there is a section for providing information about any supplements you took. Brand name, full name of supplement, strength and the amount taken should be recorded.

When to fill in the diary

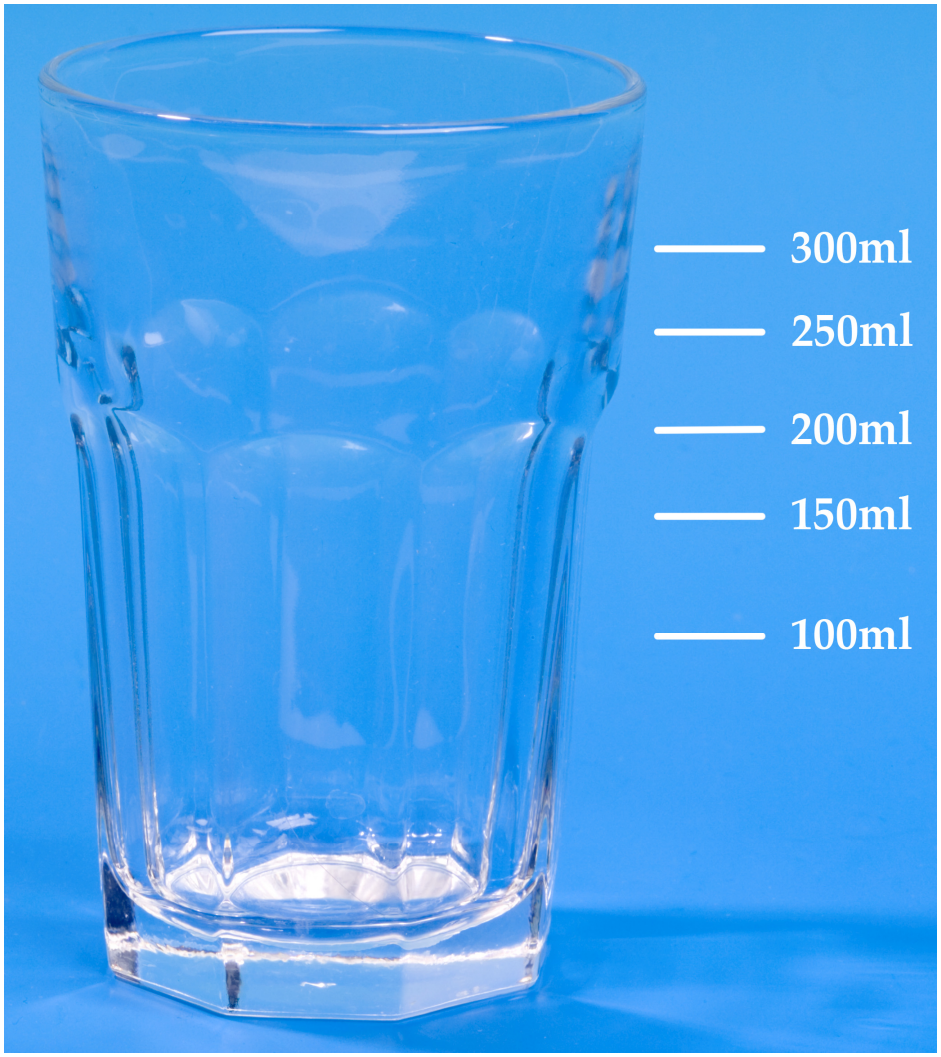
Please record your eating as you go, **not from memory** at the end of the day. Use written notes on a pad if you forget to take your diary with you. Each diary day covers a 24hr period, so please include any food or drinks that you may have had during the night. Remember to include foods and drinks between meals (snacks) including water.

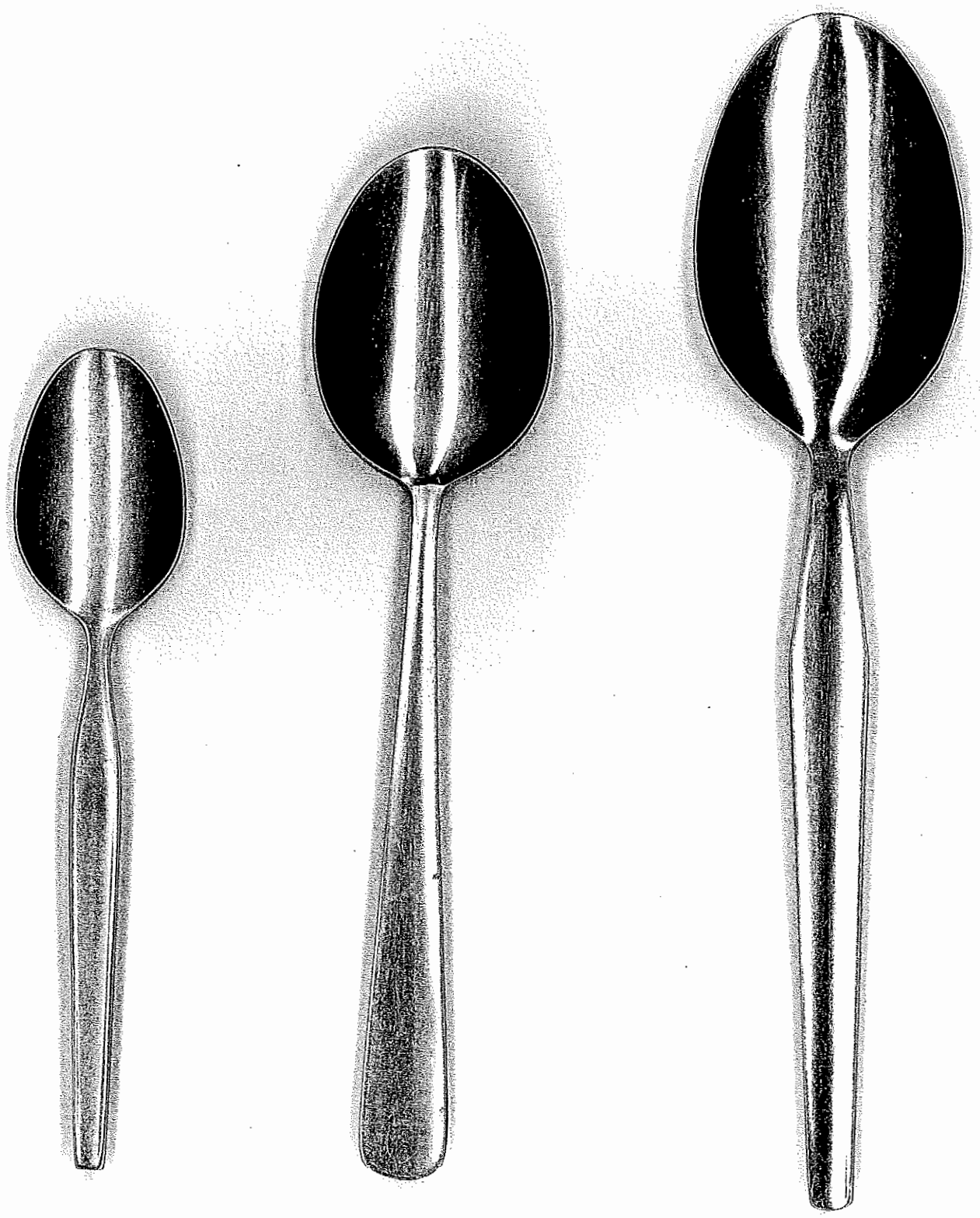
It only takes a few minutes for each eating occasion!

For your convenience a separate booklet with instructions and examples is provided.

Thank you for your time – we really appreciate it!

Life Size Glass





Teaspoon
(tsp)

Dessertspoon
(dsp)

Tablespoon
(tbsp)

DAY 1

Day of the week:

Date:

Day 1:		Date:		
Time	**Where? With Whom? TV on? At table?**	**Food/Drink description & preparation**	**Brand Name**	**Portion size or quantity <u>eaten</u>**
How to describe what you had and how much you had can be found on pages 16 - 21				
6am to 9am				
9am to 12 noon				

Time	Where? With Whom? TV on? At table?	Food/Drink description & preparation	Brand Name	Portion size or quantity <u>eaten</u>
12 noon to 2pm				
2pm to 5pm				

Time	Where? With Whom? TV on? At table?	Food/Drink description & preparation	Brand Name	Portion size or quantity <u>eaten</u>
5pm to 8pm				
8pm to 10pm				
10pm to 6am				

Was the amount of **food** that you had today about what you usually have, less than usual, or more than usual?

Yes, usual ☐ No, **less** than usual ☐ No, **more** than usual ☐

Please tell us why you had less than usual

Please tell us why you had more than usual

Was the amount you had to **drink** today, including water, tea, coffee and soft drinks [and alcohol], about what you usually have, less than usual, or more than usual?

Yes, usual ☐ No, **less** than usual ☐ No, **more** than usual ☐

Please tell us why you had less than usual

Please tell us why you had more than usual

Did you **finish all the food and drink** that you recorded in the diary today?

Yes ☐ No ☐

If no, please **go back to the diary and make a note of any leftovers**

Did you take any **vitamins, minerals or other food supplements** today?

Yes ☐ No ☐

If yes, **please describe the supplements you took below**

Brand	Name (in full) including strength	Number of pills, capsules, teaspoons

Please record on the next pages details of any recipes or (if not already described) ingredients of made up dishes or take-away dishes.

Write in recipes or ingredients of made up dishes or take-away dishes			
NAME OF DISH:		***Serves:***	
Ingredients	***Amount***	***Ingredients***	***Amount***
Brief description of cooking method			

Write in recipes or ingredients of made up dishes or take-away dishes			
NAME OF DISH:		***Serves:***	
Ingredients	***Amount***	***Ingredients***	***Amount***
Brief description of cooking method			

General questions about your food/ drink during the recording period.

Special diet

1. Did you follow a special diet during the recording period e.g. vegetarian, cholesterol lowering, weight reducing?

Yes ☐ *Please specify* No ☐

Milk

2. Which type of milk did you use most often during the recording period?

Whole, fresh, pasteurised ☐ Semi-skimmed fresh, pasteurised ☐ Skimmed (fat free) fresh, pasteurised ☐ 1% fat milk, pasteurised ☐

Dried ☐ *Type* Soya ☐ *Type*

Other ☐ *Type* Did not use ☐

Tea and coffee

3. How much milk did you usually have in coffee/ tea?

Coffee A lot ☐ Some ☐ A little ☐ None/did not drink ☐

Tea A lot ☐ Some ☐ A little ☐ None/did not drink ☐

4. Did you usually sweeten your coffee/ tea with sugar?

Coffee Yes ☐ How many teaspoons in a mug/cup? ☐ No/did not drink ☐

Tea Yes ☐ How many teaspoons in a mug/cup? ☐ No/did not drink ☐

5. Did you usually sweeten your coffee/ tea with artificial sweetener?

Coffee Yes ☐ How many tablets or teaspoons in a mug/cup? ☐ No/did not drink ☐

Tea Yes ☐ How many tablets or teaspoons in a mug/cup? ☐ No/did not drink ☐

6. Did you drink decaffeinated coffee/ tea during the recording period?

Coffee Always ☐ Sometimes ☐ Never ☐

Tea Always ☐ Sometimes ☐ Never ☐

Breakfast cereals

7. How much milk did you usually have on breakfast cereal?

Drowned ☐ Average ☐ Damp ☐ None/did not eat ☐

8. How did you usually make your porridge?

With all water ☐ With all milk ☐ With milk and water ☐ Did not eat ☐

9. Did you usually sweeten or salt your porridge?

With sugar ☐ With honey ☐ With salt ☐ Neither/did not eat ☐

10. How did you usually make your instant oat cereal?

With all water ☐ With all milk ☐ With milk and water ☐ Did not eat ☐

11. Did you usually sweeten or salt your instant oat cereal?

With sugar ☐ With honey ☐ With salt ☐ Neither/did not eat ☐

Fats for spreading and cooking

12. Which type of butter, margarine or other fat spread did you use most often during the recording period? Please record the full product name and fat content

Name:

None ☐

e.g. Flora Omega 3 plus, low fat spread, 38% fat, polyunsaturated

13. How thickly did you spread butter, margarine on bread, crackers etc?

Thick ☐ Medium ☐ Thin ☐ N/A ☐

14. Which type of cooking fat/oil did your household use most often over the recording period? Please record the full product name e.g. *Sainsbury's sunflower oil*

Name:

None ☐

Bread

15. Which type of bread did you eat most often during the recording period?

White ☐ Granary ☐ Wholemeal ☐ Brown ☐

50/50 bread e.g. Hovis Best of Both ☐ Other ☐ *Type* Did not eat ☐

16. Was it a large loaf or a small loaf?

Large ☐ Small ☐

17. If the bread was shop bought, how was it sliced?

Thick ☐ Medium ☐ Thin ☐ Unsliced ☐ N/A ☐

Meat

18. If you ate meat during the recording period, did you eat the visible fat?

Always ☐ Sometimes ☐ Never ☐ Did not eat meat ☐

19. If you ate poultry (e.g. chicken, turkey) during the recording period, did you eat the skin?

Always ☐ Sometimes ☐ Never ☐ Did not eat poultry ☐

Fruit and vegetables

20. If you ate apples during the recording period, did you eat the skin?

Always ☐ Sometimes ☐ Never ☐ Did not eat ☐

21. If you ate pears during the recording period, did you eat the skin?

Always ☐ Sometimes ☐ Never ☐ Did not eat ☐

22. If you ate new potatoes during the recording period, did you eat the skin?

Always ☐ Sometimes ☐ Never ☐ Did not eat ☐

23. If you ate baked/jacket potatoes during the recording period, did you eat the skin?

Always ☐ Sometimes ☐ Never ☐ Did not eat ☐

Salt

24. Do you add salt to your food at the table?

Always ☐ Sometimes ☐ Never ☐

25. Do you add salt substitute to your food at the table? *e.g. LoSalt*

Always ☐ Sometimes ☐ Never ☐

Water

26. Which type of water did you drink most often during the recording period?

Tap ☐ Filtered ☐ Bottled ☐ *brand* Did not drink ☐

Thank you for completing this diary.

Appendix 8 – Data collection sheet – infant visit

Subject Number:

RESEARCH WITH PLYMOUTH UNIVERSITY

Date:

Delivery date:

GA at birth:

Neonatal Anthropometry:

Birth weight: _____

Head circumference: _____

Length: _____ _____ _____

Arm circumference: _____ _____ _____

Triceps Skinfold: _____ _____ _____

Biceps Skinfold: _____ _____ _____

Subscapular Skinfold: _____ _____ _____

Method of delivery: _____

Complications during labour: _____

Feeding method: _____

Notes:

Appendix 9 – Participant nutrient intakes (excluding ‘definite’ under-reporters)

Table A1. Macronutrient intake per trimester for all women, excluding 'definite under-reporters'.

	Trimester 1 (n=49)	Trimester 2 (n=42)	Trimester 3 (n=41)
Energy			
Energy (kcal)	1946 ± 340	2000 ± 340	2063 ± 366
Carbohydrate			
Total CHO (g)	259.6 ± 51.5	251.0 {234.8-268.4}[a]	258.4 ± 58.4
Energy CHO (%)	53.6 ± 6.8	51.3 ± 6.8	50.2 ± 7.4
Starch (g)	133.2 ± 30.4	133.9 ± 32.7	134.3 ± 39.6
Total sugars (g)	105.2 {95.4 -116.0}[a]	104.6 ± 32.7	106.8 ± 45.2
Energy sugars (%)	22.0 {20.1 – 24.0}[a]	20.8 ± 6.7	20.6 ± 7.5
Total sucrose (g)	37.3 {32.5 – 42.8}[a]	35.2 {29.9 – 41.4}[a]	43.0 ± 5.0
Energy sucrose (%)	7.8 {6.8 – 8.9}[a]	7.9 ± 3.3	8.3 ± 2.7
Fibre (g)	18.2 ± 4.2	17.7 ± 4.5	18.0 ± 5.0
Fat			
Total fat (g)	75.2 ± 18.9	78.4 ± 18.2	83.9 ± 22.9
Energy fat (%)	34.6 ± 4.8	35.2 ± 5.2	36.5 ± 6.3
Saturated fat (g)	27.0 ± 8.3	28.6 ± 8.3	31.3 {28.1 – 34.8}[a]
Energy saturated fat (%)	12.4 ± 2.6	12.8 ± 2.8	14.1 {13.0 – 15.2}[a]
Protein			
Protein (g)	71.1 {66.2 – 76.3}[a]	81.2 ± 17.5	81.5 {76.6 – 86.7}
Energy protein (%)	14.8 {14.1 – 15.6}[a]	16.4 ± 3.3	16.0 {15.3 – 16.9}[a]

Mean ± SD (range)

[a]Mean calculated by back-transformation {CI}

Appendix 10 – Published literature review

MATERNAL LIFESTYLE FACTORS AND FETAL MACROSOMIA RISK: A REVIEW

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ABSTRACT

Fetal macrosomia is associated with a number of health complications for both mother and infant in the immediate, short, and long-term. Maternal obesity and excessive gestational weight gain (GWG) have long been associated with fetal macrosomia, however the impact of maternal lifestyle factors such as dietary intake and energy balance, in combination with the timing and composition of weight gain, have been less studied. It is also clear that although maternal obesity and excessive GWG increase the risk of fetal macrosomia independently, the risk is magnified with the presence of both risk factors, suggesting that interventions to control GWG may be particularly important for obese women. Association studies examining the relationship between fetal nutrient availability, epigenetic modifications, and infant anthropometrics are also required. This review provides an overview of the current evidence examining the role of maternal lifestyle factors on the prevalence of fetal macrosomia and identifies areas where further research is required in order to inform the design of appropriate intervention strategies.

Keywords: Birth weight, body composition, gestational weight gain (GWG), macrosomia, maternal obesity.

INTRODUCTION

Birth weight is a key determinant of infant health, which appears to be determined by a complex interaction of maternal and fetal factors. These probably include maternal genetic, environmental, and lifestyle factors, in conjunction with fetal genetic and intrauterine environmental factors. Macrosomia is generally defined as a birth weight >4,000 g or 4,500 g, irrespective of gestational age,[1] while large for gestational age (LGA) is defined as a birth weight >90th percentile as per gestational age.[2]

Excessive fetal growth results in increased immediate, short, and long-term risks for both mother and infant. Macrosomia increases the risk of complications during delivery such as birth asphyxia, shoulder dystocia, and increased incidence of delivery via caesarean section, which carries its own adverse risks to both neonate and mother.[3] Furthermore, higher birth weight is also associated with increased risk of obesity[4] and metabolic syndrome[5] into childhood, which have serious long-term health consequences.

Numerous maternal factors such as body mass index (BMI), gestational weight gain (GWG), diet, physical activity, and the development of gestational diabetes have all been shown to impact infant birth weight. However, previous studies have tended to examine these factors individually, and their interaction even less so. The purpose of this review is to critically appraise the current literature and highlight areas where further research is required to inform appropriate maternal intervention strategies, with the aim of improving neonatal health.

MATERNAL WEIGHT

When examined individually, high maternal pre-pregnancy BMI tends to be strongly associated with an increased risk of macrosomia. Numerous studies have reported women classified by their BMI as obese to be at a significantly greater risk of macrosomia compared with women classified as having a healthy weight,[6,7] with risk increasing as BMI increases beyond the healthy range.[8] A recent systematic review and meta-analysis

conducted by Gaudet et al.[1] showed a positive relationship between maternal obesity and fetal overgrowth as defined by birth weight ≥4,000 g, ≥4,500 g, and ≥90th percentile for gestational age.

Similarly, excessive GWG has been shown to increase risk of macrosomia.[9-11] Although it appears that both maternal obesity and excess GWG independently increase the risk of macrosomia, the interaction between the two factors is less clear. Crane et al.[12] conducted a retrospective cohort study evaluating the effects of GWG on maternal and neonatal outcomes in different BMI classes. In keeping with findings from previous studies[6-8] they observed that overweight and obese mothers were significantly more likely to give birth to a macrosomic infant (birth weight ≥4,000 g and adjusted for gestational age) and also more likely to gain excess weight than healthy weight mothers. However, when the impact of GWG on risk of macrosomic infant was examined by BMI class, risk increased with excess GWG for all BMI classes suggesting that when excessive GWG does occur, the risk of macrosomia increases regardless of pre-pregnancy BMI. A major limitation of this study was that it was retrospective, and so pre-pregnancy BMI or GWG data were missing for 47.8% of the study participants. Nohr et al.[13] conducted a similar study reporting that BMI category was a stronger predictor of LGA neonate than GWG, but that very high GWG (defined as >20 kg) increased the absolute risk of LGA neonate across all BMI categories. Limitations of the study were that pre-pregnancy weight, height, and GWG were self-reported and thus the reliability has been disputed.[14] In addition to examining the effect of maternal obesity and GWG on infant birth weight, Carlsen et al.[15] included neonatal body composition as an outcome measure. They observed that infants born to obese mothers were heavier than infants born to healthy weight mothers, and this was exclusively due to increased adiposity. GWG on the other hand, was found to increase fat mass, abdominal fat mass, and fat-free mass. Obese mothers were more likely to exhibit excessive GWG, thereby suggesting these women as a particularly important target group to receive an intervention with an aim of reducing fetal macrosomia.

The effect of GWG on maternal and neonatal outcomes in women classified as having a healthy pre-pregnancy BMI was examined by Deruelle et al.[16] Although most neonatal outcomes were similar between GWG groups, mean birth weight was significantly greater in women with ≥18 kg GWG than women gaining 9–15 kg, while the proportion of macrosomic neonates more than doubled for women with ≥18 kg GWG compared with those gaining 9–15 kg (12.1% versus 5.2%, p<0.03). Prevention of excess GWG in women of healthy pre-pregnancy BMI is therefore also important, just as in overweight or obese mothers. In 2009, the Institute of Medicine (IOM) published a new set of guidelines on GWG to replace those previously published in 1990[11] and now make recommendations based on pre-pregnancy BMI category for total and rate of weight gain.

It has been suggested that birth weight and early childhood growth patterns can lead to a predisposition to childhood obesity, with the potential to persist into adolescence and adulthood.[17] In a diverse sample of women from the USA, inadequate GWG, when compared with adequate weight gain, was associated with significantly increased odds of infants being born small for gestational age (SGA), while excessive gain was significantly associated with decreased odds of SGA and more than doubled the risk of LGA.[18] Excessive GWG also significantly increased the risk of child overweight or obesity (BMI ≥85th percentile) when followed up between the ages of 2 and 20 years. For overweight and obese women, predicted probabilities of LGA newborns and childhood overweight were higher than those for underweight or healthy weight women, regardless of GWG. Increased GWG was significantly associated with increased probability of LGA and an overweight child across all BMI groups. Similarly, a retrospective cohort of 499 mother–child dyads[19] observed that maternal morbid obesity (BMI ≥40 kg/m^2) was significantly associated with infant birth weight and weight for length throughout the first 3 months of life, and that these associations were significantly amplified by excess GWG. At 12 months of age these effects were sustained, with infants of morbidly obese mothers exhibiting an 8.4% higher weight for length percentile compared with infants of mothers with a BMI of 25 kg/m^2. Infants born to mothers with a healthy BMI but with excess GWG normalised their growth by 12 months of age.

These findings suggest that babies born to women in all BMI categories are at risk of increased birth weight and elevated weight during early life as a result of excessive GWG, but that overweight and obese women are of particular concern, as their risk appears to be amplified.[15,19] Future studies,

particularly of a prospective nature, should therefore focus on this group of women in order to develop a wider understanding of lifestyle factors that contribute to excess GWG.

MATERNAL BODY COMPOSITION

Although BMI is widely used to provide estimates of body composition, it is not without its limitations. Prentice and Jebb[20] propose that obesity should be defined as the excess accumulation of body fat, whereas BMI identifies the presence of excess body weight, which also reflects lean body mass. Krentz et al.[21] compared birth weight outcomes for women with the same BMI, but two different heights in a retrospective cohort study. They observed differences in birth weights and birth weight classification by gestational age between groups, which once again provided evidence to suggest the limited utility of BMI as a predictor of neonatal outcomes. In addition, GWG is typically reported as a single measure of mass gained during pregnancy, with the individual effects of fat mass and fat-free mass gains left undefined. It therefore seems prudent to examine the contributions of changes to estimated maternal fat mass and fat-free mass on pregnancy outcomes, in addition to total GWG and maternal obesity defined by BMI.

As might be expected, maternal weight, fat-free mass, and fat mass increased between 28 and 37 weeks gestation in a recent prospective cohort study examining maternal body composition. However, birth weight significantly correlated with maternal fat-free mass and not fat mass.[22] In a similar study, fat-free mass, but not fat mass, was also a significant predictor of birth weight and after adjustment for confounding variables, mothers in the highest fat-free mass quartile were at significantly higher risk of infant macrosomia, compared with mothers in the lowest quartile.[23] However, this study measured body composition only in the first trimester. Butte et al.[24] divided GWG into fat mass, fat-free mass, total body water, and protein gains as assessed at 9, 22, and 36 weeks of gestation. Infant birth weight was found to correlate significantly with fat-free mass ($r=0.39$, $p=0.003$) and total body water ($r=0.37$, $p=0.006$), but not fat mass ($r=0.05$, $p=0.76$). These studies suggest that fat-free mass, and not fat mass mediates an increase in infant birth weight. It is hypothesised that these positive associations between maternal fat-free mass and infant birth weight may be due to maternal plasma volume expansion,[25] which in turn is influenced by maternal hormonal changes.[26]

Forsum et al.[27] addressed the hypothesis that maternal body fat stimulates fetal growth and fat deposition. In a small, observational study they assessed infant subcutaneous adipose tissue volume *in vivo* using magnetic resonance imaging, while maternal body composition was assessed using a two-compartment model based on total body water. It was observed that maternal total body fat before pregnancy and at 32 weeks gestation was significantly and positively correlated with infant birth weight, while in infants, birth weight positively correlated with subcutaneous adipose tissue. Further studies examining the effects of maternal body composition on neonatal body composition and incidence of macrosomia are therefore required in order to fully understand the relationship between the composition of GWG and infant birth size.

TIMING OF GESTATIONAL WEIGHT GAIN

Although the influence of total GWG during pregnancy has been well documented, the timing of overnutrition and subsequent weight gain has not been examined as thoroughly. This could be an important factor in the design of any intervention studies. Davenport et al.[28] evaluated whether the timing of excessive GWG in pregnant women following current healthy living guidelines affected neonatal adiposity at birth in their prospective cohort study. The cohort was retrospectively grouped according to IOM guidelines[11] by weight gain in the first and second halves of pregnancy. Infants born to women who exhibited excessive GWG during the first half of pregnancy exhibited greater birth weight, crown–heel length, and excessive neonatal body fat compared with infants born to women who exhibited appropriate GWG in the first half of pregnancy. These differences remained significant after controlling for BMI, total GWG, maternal age, gestational age, and neonatal sex. Farah et al.[22] conducted a longitudinal prospective observational study which observed that birth weight was significantly correlated with GWG before the third trimester ($r=0.163$, $p=0.027$) but not with total or third trimester GWG. These studies suggest that neonatal adiposity is potentially more strongly influenced by timing of GWG than total GWG, suggesting a direct link between the early

intrauterine environment and subsequent neonatal adiposity. However, the data on timing of GWG and its influence on neonatal weight and adiposity is limited. Studies examining weight change during pregnancy with frequent assessments are therefore required in order to increase our understanding of the mechanism by which maternal obesity and GWG influence infant birth weight and body composition.

GESTATIONAL DIABETES MELLITUS

Gestational diabetes mellitus (GDM) is a common metabolic complication of pregnancy, defined as glucose intolerance with first onset or recognition during pregnancy.[29] GDM is most frequently observed amongst overweight or obese women[30] as these women are more likely to exhibit impaired glucose tolerance and decreased insulin sensitivity before and during pregnancy[31] when compared with women of a healthy weight. Infants born to women with GDM are often characterised by excessive fetal growth and subsequently tend to be at increased risk of macrosomia.[31] However, even in the absence of increased body mass, studies have shown that infants born to mothers with GDM exhibit increases in fat mass, but not fat-free mass when compared with women with normal glucose tolerance.[32,33] Results from the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study observed an increase in neonatal adiposity associated with increasing maternal glucose concentrations, less than those used to define GDM.[34] Physical activity has also been shown to influence glucose metabolism and transport via insulin-independent pathways and has been associated with a decreased incidence of GDM in epidemiological studies.[35]

MATERNAL ENERGY INTAKE AND EXPENDITURE

Clearly, nutritional status prior to and during pregnancy is essential for the growth and development of the fetus, with excessive GWG and adverse pregnancy outcomes also largely influenced by dietary intake either as nutrient excess, nutrient deficiencies, or by indirectly influencing the intrauterine environment. A study by Knudsen et al.[36] supports the theory that maternal glucose metabolism may impact fetal growth. They examined the associations between maternal glycaemic load, GWG, birth weight, and risk of LGA neonate as part of the Danish National Birth Cohort. They observed that the risk of LGA neonate increased by 14% for the highest glycaemic load quintile, compared with the lowest quintile. A randomised controlled trial examining the impact of a low glycaemic index diet on neonatal anthropometry observed a decrease in neonatal thigh circumference for the intervention group when compared with a control group, although no differences were observed for any skinfold measurements, nor head, abdominal, and mid-upper arm circumferences.[37]

In a prospective study, GWG was significantly and positively associated with energy intake and energy-adjusted intakes of lipids from animal origin and protein, while a significant inverse association was observed between carbohydrate intake and GWG, but these were not significantly related to birth size.[38] Olsen et al.[39] observed that milk consumption during pregnancy was inversely associated with SGA, and directly associated with LGA and mean birth weight. Women consuming ≥6 glasses of milk/day had increased risk of LGA infants when compared with women who reported no milk consumption. When fat and protein intakes from dairy products (excluding cheese and ice cream) were examined, no association between birth weight and fat intake was found, while a positive association between protein intake and birth weight was observed. The authors proposed that the positive association between milk consumption and birth weight is driven by the presence of insulin-like growth factor 1 in both low-fat and whole-milk products. Montpetit et al.[40] examined the contribution of pre-pregnancy BMI, energy intake, and physical activity as determinants of GWG and infant birth weight. Energy intake was the only significant predictor of infant birth weight. Steps per day were inversely associated with GWG, although when pre-pregnancy BMI was added to the model, steps were no longer significant and BMI remained the only significant variable.

A study conducted in the USA[41] observed decreases in birth weight and LGA births between 2000 and 2005, trends which did not appear to be explained by routinely recorded maternal characteristics. The authors hypothesised that other maternal characteristics such as maternal diet, physical activity, or socioeconomic factors may have contributed to the trends observed and called for detailed studies of smaller populations to explore the role of these factors.

Furthermore, the rapidly expanding field of epigenetic epidemiology has observed numerous associations between fetal nutrient availability and epigenetic modifications.[42] Differences in the methylation status of candidate genes have been observed in relation to fetal growth[43] and later childhood adiposity.[44,45] However, human studies examining specific intrauterine nutritional exposures and subsequent adiposity at birth and during childhood are scarce. Studies of an observational and epigenetic nature are therefore essential for increasing our understanding of how nutritional exposures influence GWG and infant phenotypic outcomes.

CONCLUSION

It is important to gain an understanding of the factors influencing neonatal anthropometric outcomes, as macrosomic infants with or without excess adiposity at birth have been shown to be at increased risk of adverse consequences such as insulin resistance,[46,47] metabolic syndrome,[5] and childhood obesity.[4,48] As observed in the current literature, there is consistent evidence to suggest that maternal obesity and excess GWG alongside GDM contribute to increased risk of adverse neonatal anthropometric outcomes;[12,13] hence current pregnancy interventions are already aiming to reduce the prevalence of these risk factors. However, maternal obesity and GWG are broad outcome measures. Recent studies suggest maternal body composition and timing of GWG may influence infant anthropometrics independently of maternal BMI and total GWG, which may offer an increased understanding of the mechanisms by which maternal obesity and GWG influence neonatal anthropometric outcomes. At present, data in this area is limited[22,23,28] and there is also a lack of recent prospective studies examining the effects of GWG by BMI according to the most recent IOM recommendations.[11]

Table 1: The contributions of maternal lifestyle factors to risk of macrosomia.

	Increased risk of macrosomia/LGA/higher birth weight		Unaffected risk of macrosomia/LGA/higher birth weight	
Factor	**Evidence?**	**References**	**Evidence?**	**References**
Maternal pre-pregnancy BMI 30 kg/m^2	Yes	1,6-8,18	No	N/A
GDM	Yes	31-34	No	N/A
Excess total GWG	Yes	9,10,16,18	Yes	22
Maternal obesity and excess total GWG	Yes	12,13,15,19	No	N/A
Early excessive GWG (first or second trimester)	Yes	22,28	No	N/A
GWG in third trimester	No	N/A	Yes	22
Maternal fat mass	Yes	27	Yes	22,24
Maternal fat-free mass	Yes	22-24	No	N/A
Dietary energy intake	Yes	40	Yes	38
Dietary fat intake	No	N/A	Yes	39,51
Dietary protein intake	Yes	39	No	N/A
Milk consumption	Yes	39	No	N/A
Glycaemic load	Yes	36,37	No	N/A
Physical activity	No	N/A	Yes	8,40

BMI: body mass index; LGA: large for gestational age; GDM: gestational diabetes mellitus; GWG: gestational weight gain; N/A: not applicable.

Maternal diet and energy balance during pregnancy undoubtedly influence GWG and subsequent anthropometric outcomes for offspring. However, despite a wealth of studies linking maternal energy intake to GWG,[38,49] and maternal dietary glucose intake to neonatal anthropometry,[36,37] few studies have examined the impact of other nutrients in the maternal diet, nor energy balance together with physical activity. Studies examining nutritional exposures during pregnancy and epigenetic modifications in offspring are also required.[50]

The contributions of various maternal lifestyle factors to fetal macrosomia from the current literature are summarised in Table 1. As discussed however, there are gaps in the current literature, as well as conflicting findings. It is therefore necessary to examine further the independent and moderating effects of maternal dietary intake, physical activity, and the timing and composition of GWG on neonatal anthropometric outcomes in future studies. Such studies could provide a more complete picture of the maternal lifestyle factors contributing to GWG, neonatal body composition, and potentially future offspring health, thus allowing health professionals to develop suitable and effective interventions to improve birth and health outcomes for both mother and infant. In the meantime, pregnant women should be advised to adhere to IOM guidelines for weight gain[11] and offered nutritional support if necessary. Particularly close attention should be paid to women entering their pregnancy with a BMI ≥30, as offspring of these women appear to be at increased risk of macrosomia, regardless of the contribution of other potential risk factors yet to be investigated.

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